Synthesis of Oxa-analogues of Zearalanone

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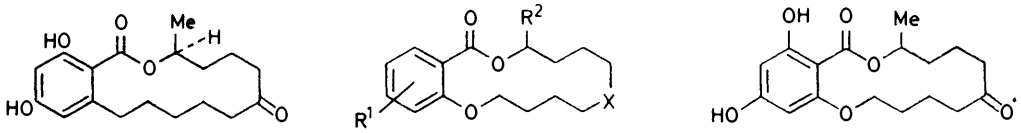
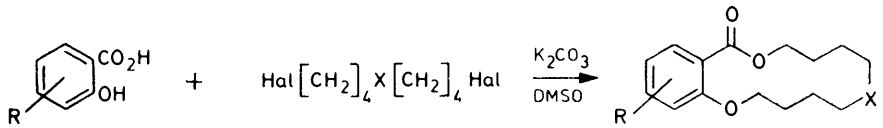
The synthesis of macrocyclic lactones related to zearalanone is described. The reaction of salicylic acids with 1,9-dibromononane, 1,9-dichloro-5-oxanonane, and 1,9-dibromononan-5-one was used to prepare the corresponding lactones. Cyclisation of 2-(9-hydroxynonyloxy)benzoic acid, 4,6-dibenzyloxy-2-(9-hydroxynonyloxy)benzoic acid, and 4-benzyloxy-2-hydroxy-6-(9-hydroxy-5-oxodecyloxy)benzoic acid using diethyl azodicarboxylate–triphenylphosphine gave the corresponding lactones in moderate yield.

ZEARALANONE (1) has been reported to exhibit both potent growth promotant activity [1] and oestrogenic activity [2] in animals. To investigate the possibility that useful anabolic activity might be retained in simpler compounds, oxa-analogues of types (2) and (3) were prepared. The synthesis of (4), which retains most of the structural features of zearalanone (1), was seen as our principal objective.



(1) (2; R^2 = H; X = CH_2, O, CO) (3; R^1 = Me, X = CO) (4)



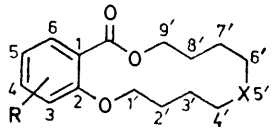
(6) (5) (2)

SCHEME 1

RESULTS AND DISCUSSION

The synthesis of target molecules (2) should be possible from readily available starting materials such as substituted salicylic acids and αω-difunctionalised nonanes. An existing technique for the lactonisation of ω-bromoalkanoic acids [3] was successfully extended to form both the ether and ester bonds in a single reaction according to Scheme 1.

The 1,9-dihalogenononanes (5) reacted with 1 mol of substituted salicylic acid (6) in DMSO solution in the presence of anhydrous potassium carbonate, giving moderate yields of the cyclic materials (2) (see Table). Where appropriate, the desired phenols (2; R = OH)

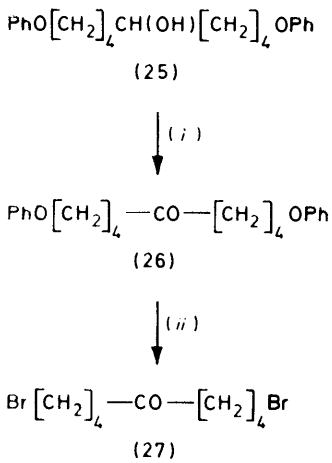


Cyclisation				Debenzylation			
Compound	R	X	Yield (%)	Compound	R	X	Yield [a] (%)
(7)	H	CH_2	27				
(8)	5-Cl	CH_2	11 [b]				
(9)	4-OCH_2Ph	CH_2	21	(18)	4-OH	CH_2	60
(10)	4,6-di-OMe	CH_2	22				
(11)	4-OCH_2Ph	O	28	(19)	4-OH	O	71
(12)	H	CO	18				
(13)	3-OCH_2Ph	CO	12 [b]	(20)	3-OH	CO	63
(14)	4-OCH_2Ph	CO	34	(21)	4-OH	CO	78
(15)	5-OCH_2Ph	CO	18	(22)	5-OH	CO	64
(16)	6-OCH_2Ph	CO	23	(23)	6-OH	CO	58
(17)	4-OCH_2Ph,6-Me	CO	20	(24)	4-OH,6-Me	CO	76

[a] Analytically pure material. [b] Yields not optimised.

were obtained by hydrogenolysis of the corresponding benzyl ethers.

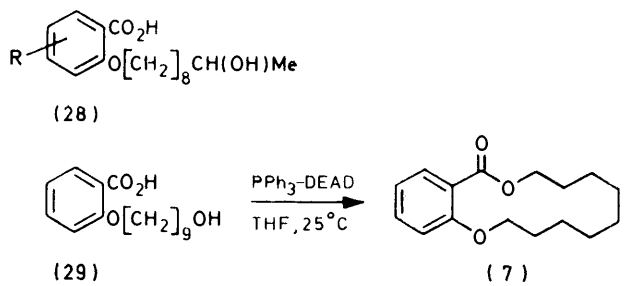
The reported synthesis of 1,9-dibromononan-5-one (27) [4] failed for large-scale preparation. A simpler scheme resulting in a high overall yield of (27) was therefore devised, and is shown in Scheme 2. The



SCHEME 2 (*i*) Jones reagent; (*ii*) $AlBr_3$

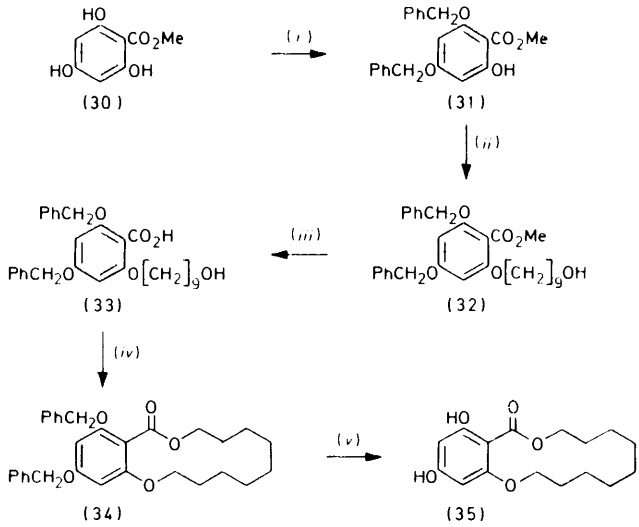
alcohol (25) [5] was oxidised using Jones reagent to the corresponding ketone (26), which was in turn converted into (27) using aluminium bromide in toluene at 110 °C. The product was not contaminated by materials derived from Friedel–Craft alkylation of toluene by the dibromo-product (27).

The above lactonisation procedure is clearly unsuitable for the synthesis of compounds of type (3). Our approach to the synthesis of such compounds required the efficient lactonisation of the seco-acid precursors (28). The cyclisation yields reported in the published



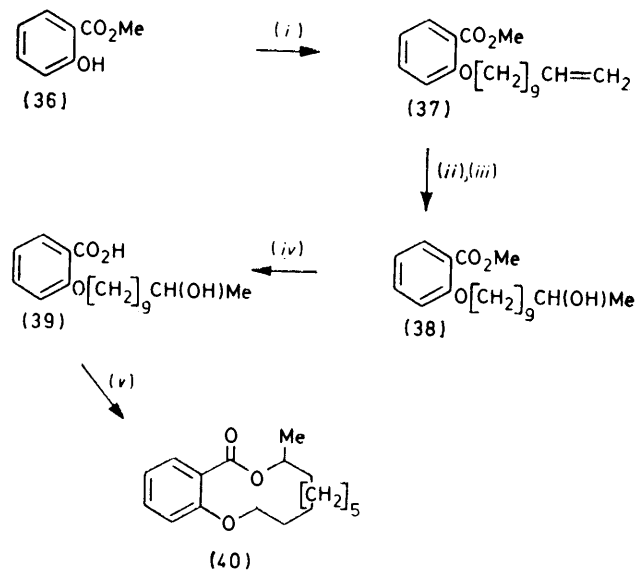
syntheses of zearalanone (1) [6,7] were low, and these routes were therefore unsuitable for our biological screening requirements. Our entry into this area coincided with the publication of the first efficient and general lactonisation procedures by Corey [8] and Masamune.[9] However, these methods each involve both the prior formation of an activated ester and the protection of any keto-function present. We therefore sought a cyclisation technique which would avoid these complications and now report that diethyl azodicarboxylate–triphenylphosphine, previously used for the synthesis of esters,[10] allowed the preparation of the required lactones (3).

In a model reaction it was found that treatment of 2-(9-hydroxynonyloxy)benzoic acid (29) with equivalent amounts of diethyl azodicarboxylate and triphenylphosphine in dry tetrahydrofuran, gave the lactone (7) in 66% yield. The generality of this procedure is shown by (*i*) synthesis of the dibenzyloxylactone (34) in 40% yield, despite the bulky *ortho*-benzyloxy-substituent (see Scheme 3); and (*ii*) applicability of this lactone



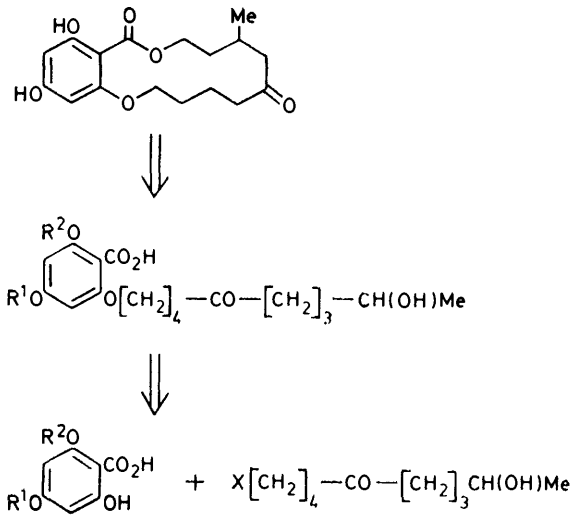
SCHEME 3 (*i*) $PhCH_2Cl$–K_2CO_3–DMF; (*ii*) $Br[CH_2]_9OH$–K_2CO_3–DMF; (*iii*) NaOH–DMSO; (*iv*) PPh_3–DEAD–THF; (*v*) Na–NH_3

synthesis to compounds having a secondary alcohol function, an example of which is shown in Scheme 4. The non-optimised yield of (40) from (39) was 20%.



SCHEME 4 (*i*) CH_2=$CH[CH_2]_9OTs$–K_2CO_3–DMF; (*ii*) $Hg(OAc)_2$–H_2O; (*iii*) $NaBH_4$; (*iv*) NaOH–MeOH; (*v*) PPh_3–DEAD–THF

Following the successful lactonisation described above, the technique was then applied to synthesis of the fully substituted racemic analogue (4). Retrosynthetic

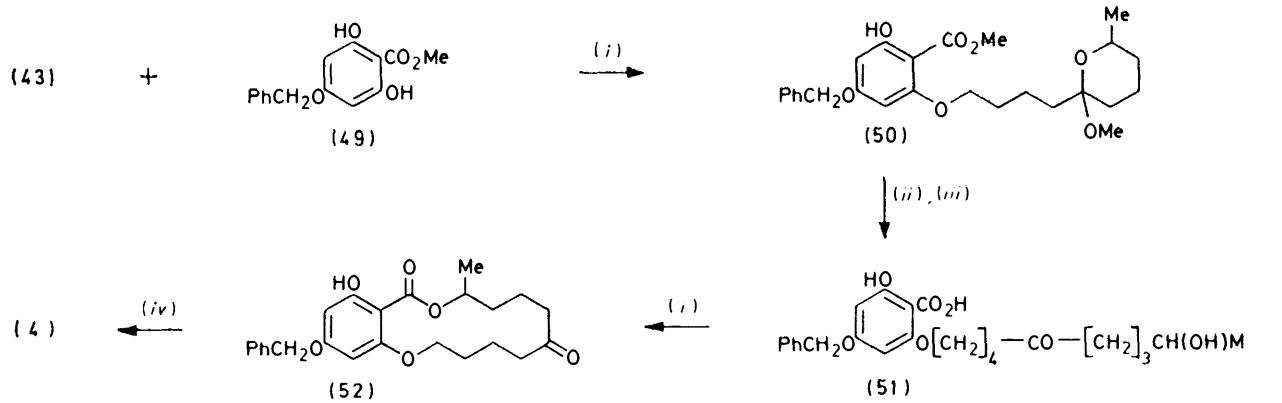


SCHEME 5

analysis (Scheme 5) and consideration of suitable protecting groups suggested as our initial target compounds the already known (41) [11] and (42), the latter previously reported as its internal acetal (43).[6]

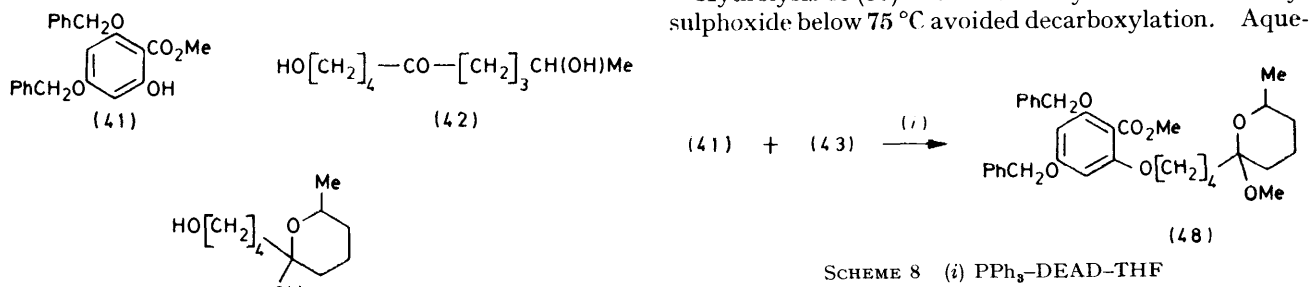
Treatment of the lactone (45) with 4-benzyloxybutylmagnesium bromide gave the keto-alcohol (46), which was cyclised under acidic conditions to the internal acetal (47). Debenzylation, with sodium–liquid ammonia, gave the alcohol (43) (Scheme 6). Coupling of (43) with (49) using diethyl azodicarboxylate–triphenylphosphine gave a good yield of the ether (50) (Scheme 7). The corresponding reaction between (41) and (43) gave only a trace of (48) (Scheme 8). This failure is probably due to the *ortho*-benzyloxy-function strengthening the intramolecular hydrogen bond present in (41). This type of selectivity of alkylation has already been reported.[12]

SCHEME 6 (*i*) Mg; (*ii*) *p*-TSA–PhMe; (*iii*) MeOH–HCl; (*iv*) Na–NH_3



SCHEME 7 (*i*) PPh_3–DEAD–THF; (*ii*) NaOH–DMSO; (*iii*) HCl–H_2O; (*iv*) H_2–Pd

Hydrolysis of (50) with sodium hydroxide in dimethyl sulphoxide below 75 °C avoided decarboxylation. Aqueous acidic work up gave the seco-acid (51) which was lactonised using diethyl azodicarboxylate–triphenylphosphine in tetrahydrofuran. The resulting lactone (52) was hydrogenolysed over a palladium catalyst to yield the target compound (4).



SCHEME 8 (*i*) PPh_3–DEAD–THF

The procedure described above provides macrocyclic lactones in acceptable yields under mild conditions. Since the completion of this work, other examples of the use of diethyl azodicarboxylate–triphenylphosphine in the synthesis of macrolides have been reported.[13,14]

The biological evaluation of these compounds is currently being undertaken.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 257 spectrophotometer. N.m.r. spectra were recorded with a Perkin-Elmer R12B instrument (60 MHz; tetramethylsilane as internal standard). Routine and high-resolution mass spectra were obtained with a VG 7070 mass spectrometer. M.p.s were determined using a Kofler hot stage apparatus. Chromatography was performed using Whatman's S13 TLC silica. All compounds reported without elemental analyses were shown to be homogeous by screening in a standard series of twenty t.l.c. systems.

1,9-dibromononane, salicylic acid, 5-chlorosalicylic acid, undecen-10-yl alcohol and methyl 2,4,6-trihydroxybenzoate were obtained from commercial sources and used without purification. 1,9-Dichloro-5-oxanonane,[15] 3-benzyloxysalicylic acid,[16] 4-benzyloxysalicylic acid,[17] 5-benzyloxysalicylic acid,[18] 6-benzyloxysalicylic acid,[12] and 4-benzyloxy-6-methylsalicylic acid [19] were prepared by reported procedures.

1,9-*Diphenoxynonan-5-one* (26).[20]—Jones reagent [21] (63 ml) was added dropwise during 1 h to a rapidly stirred solution of 1,9-diphenoxy-5-hydroxynonane (25) [5] (100 g, 0.305 mol) in acetone (1 300 ml) maintained at 0 °C. On completion of the addition, isopropyl alcohol (5 ml) was added to destroy the slight excess of Jones reagent present. The reaction mixture was filtered, the residue washed with acetone (500 ml), and the combined acetone liquors were concentrated to a small volume (*ca.* 100 ml). Water (2 000 ml) was added and the solid obtained was collected at the pump. Recrystallisation from acetone gave 1,9-diphenoxynonan-5-one (26) (75 g, 75%). An analytical sample, recrystallised from acetone–water, had m.p. 78 °C (lit., m.p. 78.5 °C) (Found: C, 77.0; H, 7.85. $C_{12}H_{26}O_3$ requires C, 77.3; H, 8.0%); $\nu_{max.}$ (KBr) 1 700 cm^{-1}; $\delta(CDCl_3)$ 1.5—1.9 (8 H, m, CH_2CH_2), 2.25—2.6 (4 H, m, CH_2COCH_2), 3.7—4.05 (4 H, m, OCH_2), and 6.6—7.4 (10 H, m, aromatic protons).

1,9-*Dibromononan-5-one* (27).[4]—Aluminium bromide (100 g, 0.37 mol) was added cautiously to a stirred solution of 1,9-diphenoxynonan-5-one (26) (60 g, 0.18 mol) in dry toluene (1 000 ml) under nitrogen. The reaction mixture was refluxed for 1 h, cooled to room temperature, then poured onto cracked ice (1 000 g) and water (1 000 ml) and the two phases separated. The aqueous phase was washed with toluene (400 ml × 2), and the combined toluene layers were washed with sodium hydroxide solution (1%, 500 ml × 4), dried ($MgSO_4$), and evaporated giving 1,9-dibromonan-5-one (27) as a pale brown oil (53 g, 96%) which was used without further purification; $\nu_{max.}$ (KBr) 1 710 cm^{-1}; $\delta(CDCl_3)$ 1.6—2.1 (8 H, m, CH_2CH_2), 2.3—2.7 (4 H, m, CH_2COCH_2), and 3.25—3.6 (4 H, m, CH_2Br).

Cyclisation Procedure.—The salicylic acid (0.1 mol) and dihalogeno-compound (0.1 mol) in dry DMSO (150 ml) were added dropwise during 4.5 h to a vigorously stirred suspension of finely divided anhydrous potassium carbonate in dry DMSO (1 000 ml) maintained at 100 °C under dry nitrogen. The reaction mixture was then heated at 100 °C with stirring for a further 2 h, cooled, diluted with water (8 000 ml) and extracted with ethyl acetate (1 000 ml × 4). The combined extracts were dried ($MgSO_4$) and evaporated leaving a pale brown oil. The oil was purified by column chromatography on Whatmans Sl3 TLC silica, eluting with chloroform.

The following compounds were prepared by the above procedure: 2-(9-*hydroxynonyloxy*)*benzoic acid lactone* (7), an oil (Found: C, 73.4; H, 8.5. $C_{16}H_{22}O_3$ requires C, 73.3; H, 8.5%); $\nu_{max.}$ (neat) 1 700 cm^{-1}; $\delta(CDCl_3)$ 1.3—2.0 (14 H, m, $C{-}CH_2{-}C$), 4.0—4.25 (2 H, m, CH_2OAr), 4.25—4.55 (2 H, m, CH_2OCO), and 6.8—7.85 (4 H, m, Ar-H).

5-*Chloro*-2-(9-*hydroxynonyloxy*)*benzoic acid lactone* (8), a white solid (from light petroleum), m.p. 74.5 °C (Found: C, 64.6; H, 7.0. $C_{16}H_{21}ClO_8$ requires C, 64.8; 7.1%); $\nu_{max.}$ (KBr) 1 725 cm^{-1}; $\delta(CDCl_3)$ 1.1—2.1 (14 H, m, $C{-}CH_2{-}C$), 3.9—4.2 (2 H, m, CH_2OAr), 4.25—4.55 (2 H, m, CH_2OCO), and 6.7—7.8 (3 H, m, Ar-H).

4-*Benzyloxy*-2-(9-*hydroxynonyloxy*)*benzoic acid lactone* (9), a white solid (from light petroleum), m.p. 77—77.5 °C (Found: C, 75.2; H, 7.7. $C_{23}H_{28}O_4$ requires C, 75.0; H, 7.7%); $\nu_{max.}$ (KBr) 1 675 cm^{-1}; $\delta(CDCl_3)$ 1.2—2.0 (14, m, $C{-}CH_2{-}C$), 3.85—4.15 (2 H, m, CH_2OAr), 4.15—4.45 (2 H, m, CH_2OCO), 5.0 (2 H, s, $PhCH_2$), 6.3—6.6 (2 H, m, 3-H and 5-H), 7.3 (5 H, s, Ph), and 7.7 (1 H, d, *J* 9 Hz, 6-H).

4,6-*Dimethoxy*-2-(9-*hydroxynonyloxy*)*benzoic acid lactone* (10), a white solid (from light petroleum), m.p. 93 °C (Found: C, 67.2; H, 8.2. $C_{18}H_{26}O_5$ requires C, 67.1; H, 8.1%); $\nu_{max.}$ (KBr) 1 730 cm^{-1}; $\delta(CDCl_3)$ 1.3—2.0 (14 H, m, $C{-}CH_2{-}C$), 3.8 (6 H, s, OMe), 3.9—4.2 (2 H, m, CH_2OAr), 4.2—4.5 (2 H, m, CH_2OCO), and 6.05 (2 H, s, Ar-H).

4-*Benzyloxy*-2-(9-*hydroxy*-5-*oxanonyloxy*)*benzoic acid lactone* (11), an oil, $\nu_{max.}$ (neat) 1 680 cm^{-1}; $\delta(CDCl_3)$ 1.6—2.2 (8 H, m, $C{-}CH_2{-}C$), 3.3—4.3 (4 H, m, CH_2OCH_2), 3.9—4.2 (2 H, m, CH_2OAr), 4.2—4.5 (2 H, m, CH_2OCO), 5.1 (2 H, s, OCH_2Ph), 6.55 (1 H, d, *J* 2 Hz, 3-H), 6.6 (1 H, dd, *J* 9, 2 Hz, 5-H), 7.4 (5 H, s, Ph), and 7.95 (1 H, d, *J* 9 Hz, 6-H) (Found: M^+, 370.418. $C_{22}H_{26}O_5$ requires *M*, 370.428).

2-(9-*Hydroxy*-5-*oxononyloxy*)*benzoic acid lactone* (12), a white solid (from isopropyl alcohol), m.p. 74 °C (Found: C, 69.4; H, 7.3. $C_{16}H_{20}O_4$ requires C, 69.5; H, 7.3%); $\nu_{max.}$ (KBr) 1 690 cm^{-1}; $\delta(CDCl_3)$ 1.6—2.1 (8 H, m, CH_2), 2.3—2.7 (4 H, m, CH_2COCH_2), 3.9—4.15 (2 H, m, CH_2OAr), 4.2—4.5 (2 H, m, CH_2OCO), and 6.7—7.8 (4 H, m, Ar-H).

3-*Benzyloxy*-2-(9-*hydroxy*-5-*oxononyloxy*)*benzoic acid lactone* (13), a white solid (from isopropyl alcohol), m.p. 74—75 °C (Found: C, 72.3; H, 6.9. $C_{23}H_{26}O_5$ requires C, 72.2; H, 6.8%); $\nu_{max.}$ (KBr) 1 695 cm^{-1}; $\delta(CDCl_3)$ 1.75—2.05 (8 H, m, CH_2), 2.35—2.7 (4 H, m, CH_2COCH_2), 4.0—4.5 (4 H, m, CH_2OAr and CH_2OCO), 5.1 (2 H, s, OCH_2Ph), 6.95—7.35 (3 H, m, Ar-H), and 7.4 (5 H, s, Ph).

4-*Benzyloxy*-2-(9-*hydroxy*-5-*oxononyloxy*)*benzoic acid lactone* (14), a white solid (from isopropyl alcohol), m.p. 103 °C (Found: C, 72.2; H, 6.9. $C_{23}H_{26}O_5$ requires C, 72.2; H, 6.8%); $\nu_{max.}$ (KBr) 1 690 cm^{-1}; $\delta(CDCl_3)$ 1.7—2.15 (8 H, m, CH_2), 2.35—2.65 (4 H, m, CH_2COCH_2), 3.9—4.15 (2 H, m, CH_2OAr), 4.2—4.4 (2 H, m, CH_2OCO), 5.1 (2 H, s, OCH_2Ph), 6.5 (1 H, d, *J* 2 Hz, 3-H), 6.55 (1 H, dd, *J* 9, 2 Hz, 5-H), 7.4 (5 H, s, Ph), and 7.85 (1 H, d, *J* 9 Hz, 6-H).

5-*Benzyloxy*-2-(9-*hydroxy*-5-*oxononyloxy*)*benzoic acid lactone* (15), a white solid (from isopropyl alcohol), m.p. 82—84 °C (Found: C, 72.5; H, 7.0. $C_{23}H_{26}O_5$ requires C, 72.2; H, 6.8%); $\nu_{max.}$ (KBr) 1 690 cm^{-1}; $\delta(CDCl_3)$ 1.7—2.1 (8 H, m, CH_2), 2.3—2.7 (4 H, m, CH_2COCH_2), 3.8—4.1

(2 H, m, CH_2OAr), 4.25—4.5 (2 H, m, CH_2OCO), 5.0 (2 H, s, OCH_2Ph), 6.7—7.4 [8 H, m (with s at 7.3), Ar-H + Ph].

6-Benzyloxy-2-(9-hydroxy-5-oxononyloxy)benzoic acid lactone (16), a white solid (from isopropyl alcohol), m.p. 74 °C (Found: C, 72.2; H, 6.9. $C_{23}H_{26}O_5$ requires C, 72.2; H, 6.8%); $\nu_{max.}$ (KBr) 1 690 cm^{-1}; $\delta(CDCl_3)$ 1.5—2.0 (8 H, m, CH_2), 2.2—2.7 (4 H, m, CH_2COCH_2), 3.8—4.1 (2 H, m, CH_2OAr), 4.2—4.55 (2 H, m, CH_2OCO), 5.05 (2 H, s, OCH_2Ph), 6.5 (2 H, dd, *J* 9, 3 Hz, 3-H and 5-H), 7.1 (1 H, d, *J* 9 Hz, 4-H), and 7.3 (5 H, s, Ph).

4-Benzyloxy-2-(9-hydroxy-5-oxononyloxy)-6-methylbenzoic acid lactone (17), an oil (Found: M^+, 396.205. $C_{24}H_{28}O_5$ requires *M*, 396.204); $\nu_{max.}$ (neat) 1 695 cm^{-1}; $\delta(CDCl_3)$ 1.5—2.0 (8 H, m, CH_2), 2.2 (3 H, s, Ar-*Me*) 2.25—2.7 (4 H, m, CH_2COCH_2), 3.8—4.1 (2 H, m, CH_2OAr), 4.2—4.45 (2 H, m, CH_2OCO), 5.1 (2 H, s, OCH_2Ph), 6.2 (2 H, br s, 3-H and 5-H), and 7.3 (5 H, s, Ph).

Hydrogenolysis.—A solution of the benzyl ether (10 mmol) in ethyl acetate (100 ml) was hydrogenated over 10% palladium–carbon (0.5 g) at a pressure of 50 lb in^{-2} at 50 °C. After the calculated amount of hydrogen had been taken up, the catalyst was removed by filtration and the filtrate evaporated, leaving a gum which was purified either by crystallisation or chromatography on silica.

The following compounds were prepared by this procedure: *4-hydroxy-2-(9-hydroxynonyloxy)benzoic acid lactone* (18), a white solid (from isopropyl alcohol–water), m.p. 134.5—135 °C (Found: C, 68.9; H, 8.3. $C_{16}H_{22}O_4$ requires C, 69.0; H, 8.0%); $\nu_{max.}$ (KBr) 3 200 and 1 640 cm^{-1}; $\delta(CDCl_3)$ 1.5—2.0 (14 H, m, $C-CH_2-C$), 3.9—4.15 (2 H, m, CH_2OAr), 4.3—4.6 (2 H, m, CH_2OCO), 6.45 (2 H, m, 3-H and 5-H), 6.5—7.5 (1 H, v.br s, OH, disappears with D_2O), and 7.75 (1 H, d, *J* 9 Hz, 6-H).

4-Hydroxy-2-(9-hydroxy-5-oxanonyloxy)benzoic acid lactone (19), a white solid (from chloroform), m.p. 110 °C (Found: C, 64.2; H, 7.32. $C_{15}H_{20}O_5$ requires C, 64.3; H, 7.2%); $\nu_{max.}$ (KBr) 3 150 and 1 680 cm^{-1}; $\delta(CDCl_3)$ 1.6—2.3 (8 H, m, CH_2), 3.5—3.8 (4 H, m, CH_2OCH_2), 3.9—4.2 (2 H, m, CH_2OAr), 4.25—4.55 (2 H, m, CH_2OCO), 6.35—6.6 (2 H, m, 3-H and 5-H), 7.85 (1 H, br s, OH, disappears with D_2O), and 7.87 (1 H, d, *J* 9 Hz, 6-H).

3-Hydroxy-2-(9-hydroxy-5-oxononyloxy)benzoic acid lactone (20), a white solid (from light petroleum), m.p. 112—114 °C (Found: C, 65.4; H, 6.6. $C_{16}H_{20}O_5$ requires C, 65.7; H, 6.9%); $\nu_{max.}$ (KBr) 3 400 and 1 700 cm^{-1}; $\delta(CDCl_3)$ 1.6—2.1 (8 H, m, $C-CH_2-C$), 2.3—2.7 (4 H, m, CH_2COCH_2), 3.8—4.2 (2 H, m, CH_2OAr), 4.3—4.6 (2 H, m, CH_2OCO), 6.3 (1 H, br s, OH, disappears with D_2O), and 7.0—7.45 (3 H, m, Ar-H).

4-Hydroxy-2-(9-hydroxy-5-oxonyloxy)benzoic acid lactone (21), a white solid (from isopropyl alcohol), m.p. 111—113 °C (Found: C, 66.1; H, 7.1. $C_{16}H_{20}O_5$ requires C, 65.7; H, 6.9%); $\nu_{max.}$ (KBr) 3 300 and 1 685 cm^{-1}; $\delta(CDCl_3)$ 1.7—2.15 (8 H, m, $C-CH_2-C$), 2.4—2.8 (4 H, m, CH_2COCH_2), 3.9—4.2 (2 H, m, CH_2OAr), 4.3—4.5 (2 H, m, CH_2OCO), 6.4—6.6 (2 H, m, 3-H and 5-H), and 7.8 (1 H, d, *J* 9 Hz, 6-H).

5-Hydroxy-2-(9-hydroxy-5-oxononyloxy)benzoic acid lactone (22), a white solid (from chloroform), m.p. 100—102 °C (Found: C, 65.8 ; H, 7.0. $C_{16}H_{20}O_5$ requires C, 65.7; H, 6.9%); $\nu_{max.}$ (KBr) 3 250 and 1 680 cm^{-1}; $\delta(CDCl_3)$ 1.7—2.2 (8 H, m, $C-CH_2-C$), 1.4—1.8 (4 H, m, CH_2COCH_2), 3.75 (1 H, s, OH, disappears with D_2O), 3.9—4.2 (2 H, m, CH_2OAr), 4.3—4.6 (2 H, m, CH_2OCO), 6.9—7.1 (2 H, m, 3-H and 4-H), and 7.4 (1 H, d, *J* 3 Hz, 6-H).

6-Hydroxy-2-(9-hydroxy-5-oxononyloxy)benzoic acid lactone (23), an oil (Found: M^+, 292.131. $C_{16}H_{20}O_5$ requires *M*, 292.131); $\nu_{max.}$ (neat) 3 100 (broad) and 1 700 cm^{-1}; $\delta(CDCl_3)$ 1.6—2.0 (8 H, m, $C-CH_2-C$), 2.2—2.7 (4 H, m, CH_2COCH_2), 3.85—4.1 (2 H, m, CH_2OAr), 4.2—4.5 (2 H, m, CH_2OCO), 6.25—6.65 (2 H, m, 3-H and 5-H), 7.0—7.3 (2 H, m, including s which disappears with D_2O, 4-H and OH).

4-Hydroxy-2-(9-hydroxy-5-oxononyloxy)-6-methylbenzoic acid lactone (24), a gum (Found: M^+, 306.150. $C_{17}H_{22}O_5$ requires *M*, 306.147); $\nu_{max.}$ ($CHCl_3$ solution) 3 300 and 1 700 cm^{-1}; $\delta(CDCl_3)$ 1.5—2.1 (8 H, m, $C-CH_2-C$), 2.15 (3 H, s, Ar-*Me*), 2.3—2.7 (4 H, m, CH_2COCH_2), 3.8—4.1 (2 H, m, CH_2OAr), 4.3—4.6 (2 H, m, CH_2OCO), and 6.25 (2 H, s, 3-H and 5-H).

2-(9-Hydroxynonyloxy)benzoic Acid (29).—To a solution of 2-(9-hydroxynonyloxy)benzoic acid lactone (7) (0.524 g, 2 mmol) in DMSO (10 ml) was added freshly prepared sodium hydroxide solution (40%, 2.5 ml), and the mixture was heated and stirred under nitrogen at 120 °C for 4 h. The reaction mixture was poured onto cracked ice (50 g) and water (50 ml). The resulting solution was acidified with dilute hydrochloric acid and then extracted with chloroform (50 ml × 3). The combined chloroform extracts were washed with water (30 ml × 3), dried ($MgSO_4$), and evaporated to give an *oil* (0.28 g, 50%) which crystallised on trituration with petroleum. An analytical sample, recrystallised from isopropyl alcohol–petroleum had m.p. 68 °C (Found: C, 68.5; H, 8.65. $C_{16}H_{24}O_4$ requires C, 68.54; H, 8.63%); $\nu_{max.}$ (KBr) 3 300 (broad) and 1 730 cm^{-1}; $\delta(CDCl_3)$ 1.2—2.0 (14 H, m, $C-CH_2-C$), 3.5—3.8 (2 H, m, CH_2OH), 4.1—4.4 (2 H, m, $ArOCH_2$), 5.5—6.2 (1 H, br s, OH, disappears with D_2O), 6.9—7.7 (3 H, m, 3-H, 4-H, 5-H), and 8.05—8.25 (1 H, m, 6-H).

2-(9-Hydroxynonyloxy)benzoic Acid Lactone (7) (*DEAD–TPP Procedure*).—To a solution of 2-(9-hydroxynonyloxy)-benzoic acid (29) (70 mg, 0.25 mmol) and triphenylphosphine (98 mg, 0.375 mmol) in dry tetrahydrofuran (5 ml) at room temperature under an atmosphere of nitrogen was added a solution of diethyl azodicarboxylate (65 mg, 0.375 mmol) in dry tetrahydrofuran (5 ml) over a period of 30 min. The mixture was stirred for a further 1 h, and the solvent then removed leaving a semi-crystalline gum. The gum was extracted with hot petroleum (b.p. 60—80 °C) (30 ml × 10), and the combined extracts were evaporated leaving 2-(9-hydroxynonyloxy)benzoic acid lactone (7) as a viscous oil (43 mg, 66%), identical in all respects to that reported above.

Methyl 4,6-Bisbenzyloxy-2-(9-hydroxynonyloxy)benzoate (32).—A stirred solution of methyl 4,6-bisbenzyloxy-2-hydroxybenzoate (31) [11] (10 g, 0.027 mol) and 9-bromononanol [22] (6.6 g, 0.027 mol) in anhydrous dimethylformamide (200 ml) containing a suspension of finely divided anhydrous potassium carbonate (7.4 g, 0.054 mol) was heated at 100 °C for 10 h under a dry nitrogen. The reaction mixture was filtered and the filtrate evaporated under reduced pressure leaving a mobile yellow oil. The oil was poured into water (500 ml) and extracted with ethyl acetate (100 ml × 3). The combined extracts were dried ($MgSO_4$) and evaporated leaving a pale yellow oil. The oil was purified chromatographically using chloroform as eluant to give methyl 2,4-bisbenzyloxy-6-(9-hydroxynonyloxy)benzoate (32) (8 g, 57%) as an amorphous white *solid*. An analytical sample, crystallised from light petroleum, had m.p. 55—56 °C (Found: C, 73.2; H, 7.6. $C_{31}H_{38}O_6$ requires C, 73.44; H, 7.56%); $\nu_{max.}$ (KBr)

3 450 (broad) and 1 725 cm^{-1}; δ($CDCl_3$) 1.2—1.9 (15 H, m, C-CH_2-C and OH, disappears with D_2O), 3.4—3.7 (2 H, m, ArOCH_2), 3.7—4.2 (5 H, m, CH_2OH + OMe), 4.95 (2 H, s, OCH_2Ph), 5.0 (2 H, s, OCH_2Ph), 6.15 (2 H, s, Ar-H), and 7.3 (10 H, s, CH_2*Ph*).

4,6-*Bisbenzyloxy*-2-(9-*hydroxynonyloxy*)*benzoic Acid* (33).—A mixture of methyl 4,6-bisbenzyloxy-2-(9-hydroxynonyloxy)benzoate (32) (7 g, 0.013 8 mol), sodium hydroxide (2.21 g, 0.055 mol), dimethyl sulphoxide (50 ml), and water (50 ml) was heated at 100 °C for 12 h under nitrogen. The white precipitate was filtered off and suspended in water (100 ml) which was acidified to pH 1 with concentrated hydrochloric acid and then extracted with chloroform (100 ml × 3). The combined chloroform extracts were dried ($MgSO_4$) and evaporated leaving a white *solid* (4.8 g, 54%). An analytical sample, recrystallised from chloroform–petroleum, had m.p. 85 °C (Found: C, 72.95; H, 7.25. $C_{30}H_{36}O_6$ requires C, 73.14; H, 7.37%); $\nu_{max.}$ (KBr) 3 400 (broad) and 1 685 cm^{-1}; δ($CDCl_3$) 1.5—1.75 (15 H, m, C-CH_2-C and OH, disappears with D_2O), 3.5—3.8 (2 H, m, ArOCH_2), 3.85—4.1 (2 H, m, CH_2OH), 4.95 (2 H, s, OCH_2Ph), 5.05 (2 H, s, OCH_2Ph), 5.15 (1 H, br s, CO_2H, disappears with D_2O), 6.15 (2 H, s, Ar-H), and 7.3 (10 H, s, OCH_2*Ph*).

4,6-*Bisbenzyloxy*-2-(9-*hydroxynonyloxy*)*benzoic Acid Lactone* (34).—To a stirred solution of 4,6-bisbenzyloxy-2-(9-hydroxynonyloxy)benzoic acid (33) (2.0 g, 0.0041 mol) and triphenylphosphine (1.13 g, 0.0043 mol) in dry tetrahydrofuran (150 ml) at 0 °C under dry nitrogen was added, during 30 min, a solution of diethyl azodicarboxylate (1.0 g, 0.0058 mol) in dry tetrahydrofuran (20 ml). The reaction mixture was allowed to warm to room temperature and stirring continued for 24 h. The tetrahydrofuran was removed *in vacuo*, and the residue triturated with ether. The mixture was cooled to 0 °C, ether (100 ml) was added, and it was set aside for 24 h. The crystalline by-products were removed by filtration, and the filtrate evaporated leaving a pale yellow oil which was purified by chromatography using chloroform as eluant. 4,6-*Bisbenzyloxy*-2-(9-*hydroxynonyloxy*)*benzoic acid lactone* (34) (1.05 g, 54%) was obtained as a colourless oil (Found: M^+, 474.242. $C_{30}H_{34}O_5$ requires *M*, 474.240); $\nu_{max.}$ (neat) 1 720 cm^{-1}; δ($CDCl_3$) 1.2—1.9 (14 H, m, C-CH_2-C), 3.8—4.1 (2 H, m, ArOCH_2), 4.2—4.5 (2 H, m, CO_2CH_2), 4.95 (2 H, s, OCH_2Ph), 5.00 (2 H, s, OCH_2Ph), 6.05 (2 H, s, Ar-H), and 7.3 (10 H, s, OCH_2*Ph*).

4,6-*Dihydroxy*-2-(9-*hydroxynonyloxy*)*benzoic Acid Lactone* (35).—To a solution of sodium (0.090 g, 0.004 mol) in redistilled liquid ammonia (20 ml) was added a solution of 4,6-bisbenzyloxy-2-(9-hydroxynonyloxy)benzoic acid lactone (34) (0.474 g, 0.001 mol) in dry xylene (10 ml), and the mixture was stirred at reflux for 1 h. Ammonium chloride (0.5 g) was added, and the ammonia allowed to evaporate. The residue was partitioned between sodium hydroxide solution (20 ml, 5%) and dichloromethane (20 ml). The aqueous layer was separated, adjusted to pH 7 with dilute hydrochloric acid, and extracted with dichloromethane (20 ml × 3). The combined dichloromethane extracts were dried ($MgSO_4$) and evaporated leaving 4,6-dihydroxy-2-(9-hydroxynonyloxy)benzoic acid lactone (35) as a white *solid* (0.251 g, 85%). An analytical sample recrystallised from chloroform–light petroleum had m.p. 125—126 °C (Found: C, 65.35; H, 7.55. $C_{16}H_{22}O_5$ requires C, 65.28; H, 7.53%); $\nu_{max.}$ (KBr) 3 500 and 1 620 cm^{-1}; δ($CDCl_3$) 1.45—1.95 (14 H, m, C-CH_2-C), 2.85 (1 H, br s, OH, disappears with D_2O), 3.9—4.15 (2 H, m, ArOCH_2), 4.25—4.5 (2 H, m, CO_2CH_2), 5.9—6.05 (2 H, m, Ar-H), and 12.1 (1 H, s, OH, disappears with D_2O).

Methyl 2-(*Undec*-10-*enyloxy*)*benzoate* (37).—A solution of methyl salicylate (1.52 g, 0.01 mol) and undec-11-enyl toluene-*p*-sulphonate [23] (3.2 g, 0.01 mol) in dry dimethylformamide containing a suspension of finely divided anhydrous potassium carbonate (2.76 g, 0.02 mol) was stirred at 100 °C under nitrogen for 5 h. The solvent was removed under reduced pressure, and the oily residue was partitioned between water (50 ml) and chloroform (50 ml). The aqueous phase was separated and re-extracted with chloroform (50 ml). The combined organic extracts were washed with aqueous sodium carbonate solution (50 ml, 5%, ×2) and water (50 ml), dried ($MgSO_4$), and evaporated leaving methyl 2-(undec-10-enyloxy)benzoate (37) (2.1 g, 70%) as a colourless mobile oil which was used without further purification (Found: M^+, 304.201. $C_{19}H_{28}O_3$ requires *M*, 304.203); $\nu_{max.}$ (neat) 1 735 and 1 640 cm^{-1}; δ($CDCl_3$) 1.25—2.25 (16 H, m, CH_2), 3.75—4.25 (5 H, m containing singlet at 3.85, OCH_2 and CO_2Me), 4.75—5.15 (2 H, m, CH=CH_2), 5.45—6.15 (1 H, m, C*H*=CH_2), and 6.6—7.85 (4 H, m, Ar-H).

2-(10-*Hydroxyundecyloxy*)*benzoic Acid* (39).—A solution of methyl 2-(undec-10-enyloxy)benzoate (37) (3.04 g, 0.01 mol) in tetrahydrofuran (5 ml) was added to a stirred suspension of mercury(II) acetate (3.19 g, 0.01 mol) in tetrahydrofuran (10 ml) and water (10 ml) at room temperature under nitrogen, and stirring was continued for 30 min. Sodium hydroxide solution (10 ml, 3N) was added followed by sodium borohydride (10 ml of 0.5M solution in 3N sodium hydroxide), and the mixture was stirred for 10 min. Brine (30 ml) was added, and the organic phase was separated, dried (Na_2SO_4), and evaporated. The oil was taken up in chloroform (100 ml), filtered, and re-evaporated leaving a pale yellow viscous oil. The oil was dissolved in methanol (40 ml) and aqueous sodium hydroxide solution (20 ml, 3N), and the mixture was refluxed for 2 h during which time a solid precipitated. The precipitate was filtered off, washed with cold methanol (10 ml), and suspended in water (20 ml). Upon acidification with dilute hydrochloric acid, a pale yellow oil separated and was extracted with chloroform (20 ml × 3). The combined organic extracts were washed with brine (20 ml), dried (Na_2SO_4), and evaporated giving 2-(10-hydroxyundecyloxy)benzoic acid (39) (1.8 g, 58%) as a pale yellow viscous oil which was used without further purification (Found: M^+, 308.199. $C_{18}H_{28}O_4$ requires *M*, 308.198); $\nu_{max.}$ (neat) 3 300 (broad) and 1 720 (broad cm^{-1}; δ($CDCl_3$) 1.15 (3 H, d, *J* 6 Hz, CH*Me*), 1.32 (16 H, br s, C-CH_2-C), 4.1—4.5 (3 H, m, OCH_2 and C*H*Me), 6.5 (2 H, br s disappears with D_2O), and 6.9—8.3 (4 H, m, Ar-H).

2-(10-*Hydroxyundecyloxy*)*benzoic Acid Lactone* (40).—A solution of diethyl azodicarboxylate (0.68 g, 0.003 9 mol) in dry tetrahydrofuran (30 ml) was added dropwise during 30 min to a stirred solution of triphenylphosphine (1.03 g, 0.003 9 mol) and 2-(10-hydroxyundecyloxy)benzoic acid (39) (1.2 g, 0.003 9 mol) at 0 °C under nitrogen. The mixture was allowed to warm to room temperature and stirred for 24 h. The solvent was removed under reduced pressure, and the resulting paste was purified chromatographically using chloroform as eluant. Combination of the relevant fractions gave, upon evaporation, 2-(10-hydroxyundecyloxy)benzoic acid lactone (40) as a colourless viscous oil (0.226 g, 20%) (Found: M^+, 290.190. $C_{18}H_{26}O_3$ requires *M*, 290.188); $\nu_{max.}$ (neat) 1 725 cm^{-1}; δ($CDCl_3$)

1.0—1.9 (19 H, m, C-CH_2-C and CH*Me*), 3.6—4.1 (2 H, m, OCH_2), 4.9—5.3 (1 H, m, C*H*Me), and 6.5—7.7 (4 H, m, Ar-H).

2-(4-*Benzyloxybutyl*)-2-*methoxy*-6-*methyltetrahydropyran* (47).—To a stirred suspension of magnesium turnings (12 g, 0.5 mol) in dry ether (250 ml) under nitrogen was added a solution of 4-benzyloxybutyl bromide (44) [24] (97.1 g, 0.4 mol) in dry ether (250 ml) at such a rate that a gentle reflux was maintained. After completion of the addition, the mixture was refluxed for 2 h. The resulting solution was added to a stirred solution of 5-hydroxyhexanoic acid lactone (45) [6] (45.1 g, 0.4 mol) in dry ether (250 ml) at 0 °C under nitrogen, and the mixture allowed to warm to room temperature. After a further 2 h stirring at room temperature, the reaction was quenched by the careful addition of saturated ammonium chloride solution until the ether layer was transparent. The ether layer was separated and the aqueous layer extracted with ether (200 ml × 2). The combined ether layers were washed with sodium hydroxide solution (100 ml, 5%), saturated ammonium chloride solution (100 ml), and saturated sodium chloride solution (100 ml), dried (Na_2SO_4), and evaporated. The oil thus obtained was dissolved in dry toluene (500 ml) containing toluene-*p*-sulphonic acid (0.5 g, 0.003 mol) and the mixture was refluxed with azeotropic removal of water for 3 h. The toluene was evaporated and the residual oil was distilled under high vacuum. The fraction boiling in the range 50—65 °C at 0.05 mmHg was dissolved in methanolic hydrogen chloride (1%, 800 ml) and the solution allowed to stand at room temperature for 16 h. The solution was neutralised by the addition of solid sodium hydrogencarbonate, filtered, and evaporated. Ether (500 ml) was added and the solution was filtered and evaporated to give 2-(4-benzyloxybutyl)-2-methoxy-6-methyltetrahydropyran (47) as an oil (101 g, 87%); δ($CDCl_3$) 1.0—2.0 (15 H, m with d at 1.14, *J* 6.5 Hz, OCH*Me* and C-CH_2-C), 3.1 (3 H, s, O*Me*), 3.2—3.8 (3 H, m, OCH_2 and O*CH*Me), 4.41 (2 H, s, O*CH*$_2$Ph), and 7.2 (5 H, s, Ar-H).

2-(4-*Hydroxybutyl*)-2-*methoxy*-6-*methyltetrahydropyran* (43).—To a stirred solution of 2-(4-benzyloxybutyl)-2-methoxy-6-methyltetrahydropyran (47) (12.5 g, 0.043 mol) in refluxing liquid ammonia (150 ml) were added small pieces of sodium (2 g), and the resulting blue-black solution was stirred for 1 h. Solid ammonium chloride was added to destroy the excess of sodium, and the ammonia was allowed to evaporate. The residue was taken up in water (400 ml) and extracted with ether (100 ml × 3). The combined extracts were dried ($MgSO_4$) and evaporated to give 2-(4-hydroxybutyl)-2-methoxy-6-methyltetrahydropyran (43) (7.3 g, 84%) as a pale yellow oil which was used without further purification; $\nu_{max.}$ (neat) 3 400 cm^{-1}; δ($CDCl_3$) 1.15 (3 H, d, *J* 7 Hz, CH*Me*), 1.2—1.85 (12 H, m, C-*CH*$_2$-C), 1.9 (1 H, s, disappears with D_2O, OH), 3.15 (3 H, s, OMe), and 3.5—3.9 (3 H, m, C*H*Me and OCH_2).

Methyl 4-*Benzyloxy*-2,6-*dihydroxybenzoate* (49).—A stirred suspension of anhydrous potassium carbonate (19.3 g, 0.14 mol) in dry acetonitrile (100 ml) containing methyl 2,4,6-trihydroxybenzoate (12.5 g, 0.07 mol) and benzyl chloride (8.25 g, 0.07 mol) was heated at 60 °C under nitrogen for 6 h. The reaction mixture was filtered and evaporated. The residue was taken up in ethyl acetate (250 ml) and extracted firstly with sodium carbonate solution (10%, 100 ml × 2) and then with sodium hydroxide solution (5%, 100 ml × 2). The combined sodium hydroxide layers were acidified with dilute hydrochloric acid and extracted with ethyl acetate (100 ml × 2). The combined organic extracts were washed with water (100 ml) and saturated sodium chloride solution (100 ml), dried ($MgSO_4$), and evaporated. The resulting *solid* was recrystallised from isopropyl alcohol (4.5 g, 23%). An analytical sample, recrystallised from isopropyl alcohol, had m.p. 117—118 °C (Found: C, 65.55; H, 5.1. $C_{15}H_{14}O_5$ requires C, 65.68; H, 5.14%); $\nu_{max.}$ (KBr) 3 300 and 1 660 cm^{-1}; δ($CDCl_3$) 3.95 (3 H, s, OMe), 5.0 (2 H, s, OCH_2), 6.0 (2 H, s, Ar-H), 7.3 (5 H, s, CH_2*Ph*), 9.8 (2 H, br s, disappears with D_2O, OH).

Methyl 4-*Benzyloxy*-6-*hydroxy*-2-[4-(2-*methoxy*-6-*methyltetrahydropyran*-2-*yl*)*butoxy*]*benzoate* (50).—Diethyl azodicarboxylate (30 g, 0.172 mol) was added dropwise during 4 h to a stirred solution of methyl 4-benzyloxy-2,6-dihydroxybenzoate (49) (37.8 g, 0.138 mol), 2-(4-hydroxybutyl)-2-methoxy-6-methyltetrahydropyran (43) (27.8 g, 0.138 mol) and triphenylphosphine (45.2 g, 0.172 mol) in dry tetrahydrofuran (750 ml) at 0 °C under nitrogen. The mixture was then allowed to warm to room temperature and stirring continued for 48 h. The solvent was then evaporated, the residue triturated with ether, and the solid by-products removed by filtration. The filtrate was evaporated, and the residue triturated with methanol (200 ml). The solid thus obtained was recrystallised from methanol to give methyl 4-benzyloxy-6-hydroxy-2-[4-(2-methoxy-6-methyltetrahydropyran-2-yl)butoxy]benzoate (50) (41.3 g, 65%) as a white crystalline solid. An analytical sample, recrystallised from methanol, had m.p. 95—100 °C (Found: C, 67.65; H, 7.3. $C_{26}H_{34}O_7$ requires C, 68.10; H, 7.47%); $\nu_{max.}$ (KBr) 1 660 cm^{-1}; δ($CDCl_3$) 1.16 (3 H, d, *J* 7 Hz, CH*Me*), 1.3—2.0 (12 H, m, C-CH_2-C), 3.2 (3 H, s, OMe), 3.8—4.15 (6 H, m, with s at 3.95, ArO*CH*$_2$, C*H*Me and CO_2Me), 5.05 (2 H, s, O*CH*$_2$Ph), 6.1 (2 H, dd, *J* 7, 2 Hz, Ar-H), 7.4 (5 H, s, CH_2*Ph*), and 12.0 (1 H, s, disappears with D_2O, OH).

4-*Benzyloxy*-6-*hydroxy*-2-(9-*hydroxy*-5-*oxodecyloxy*)*benzoic Acid Lactone* (52).—A solution of methyl 4-benzyloxy-6-hydroxy-2-[4-(2-methoxy-6-methyltetrahydropyran-2-yl)butoxy]benzoate (50) (0.625 g, 0.001 4 mol) in DMSO (40 ml) containing sodium hydroxide solution (10M; 1 ml) was heated at 70 °C for 6 h under nitrogen. The reaction was poured onto ice (50 g) and water (50 ml) and carefully acidified with dilute hydrochloric acid. The aqueous suspension was extracted with ethyl acetate (50 ml × 3), and the combined organic extracts were dried ($MgSO_4$) and evaporated leaving a gum (0.5 g). The gum was dissolved in dry tetrahydrofuran (50 ml) containing triphenylphosphine (0.61 g, 0.002 3 mol) and a solution of diethyl azodicarboxylate (0.303 g, 0.001 25 mol) in dry tetrahydrofuran (25 ml) was added dropwise with stirring over a period of 1 h. After the addition was complete, stirring was continued at room temperature for 2 h. The reaction mixture was evaporated, and the residue triturated with ether (50 ml). The resulting precipitate was filtered off, the filtrate evaporated, and the crude product so obtained was purified by preparative t.l.c. on silica, eluting with chloroform. Extraction of the band at R_F 0.45 with ethyl acetate gave 4-benzyloxy-6-hydroxy-2-(9-hydroxy-5-oxodecyloxy)benzoic acid lactone (52) (0.073 g, 15%). An analytical sample recrystallised from ethyl acetate–light petroleum (b.p. 60—80 °C) had m.p. 131 °C (Found: C, 69.65; H, 6.75. $C_{24}H_{28}O_6$ requires C, 69.88, H, 6.84%); $\nu_{max.}$ (KBr) 1 690 and 1 640 cm^{-1}; δ($CDCl_3$) 1.32 (3 H, d, *J* 7 Hz, CH*Me*), 1.5—2.2 (8 H, m, C-CH_2-C), 2.2—2.9 (4 H, m, CH_2COCH_2), 4.0 (2 H, m, ArO*CH*$_2$), 5.0—5.3 (3 H,

m, containing s at 5.05, OC*H*Me and OCH_2Ph), 6.1 (2 H, dd, *J* 7, 2 Hz, Ar-H), 7.4 (5 H, s, CH_2*Ph*), and 12.3 (1 H, s, disappears with D_2O, OH).

4,6-*Dihydroxy*-2-(9-*hydroxy*-5-*oxodecyloxy*)*benzoic Acid Lactone* (4).—A solution of 4-benzyloxy-6-hydroxy-2-(9-hydroxy-5-oxodecyloxy)benzoic acid lactone (52) (0.915 g, 0.002 8 mol) in ethanol (30 ml) was hydrogenated over 5% palladium–carbon (0.5 g) at 50 lb in^{-2} and 50° C. When the calculated amount of hydrogen had been absorbed, the catalyst was removed by filtration and the filtrate evaporated. The solid so obtained was recrystallised from ethyl acetate–light petroleum (b.p. 60—80 °C) giving 4,6-dihydroxy-2-(9-hydroxy-5-oxodecyloxy)benzoic acid lactone (4) (0.53 g, 74%) as colourless crystals. An analytical sample recrystallised from ethyl acetate had m.p. 182—183 °C (Found: C, 63.15; H, 6.85. $C_{17}H_{22}O_6$ requires C, 63.34; H, 6.88%); $\nu_{max.}$ (KBr) 3 250, 1 685, and 1 635 cm^{-1}; δ($CDCl_3$) 1.3 (3 H, d, *J* 7 Hz, CH*Me*), 1.5—2.2 (8 H, m, C-CH_2-C), 2.2—3.0 (4 H, m, CH_2COCH_2), 3.8—4.2 (2 H, m, ArOCH_2), 4.9—5.3 (1 H, m, *CH*Me), 5.95 (2 H, dd, *J* 7, 2 Hz, Ar-H), 6.4—6.8 (1 H, m, disappears with D_2O, OH), and 12.2 (1 H, s, disappears with D_2O, OH).

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