1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl acetate, 17497-46-0; 1-allylcarbinyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl acetate, 17497-47-1.

Acknowledgment.—The authors are grateful to Professor J. Meinwald for many helpful discussions and to A. J. Poje for technical assistance.

Total Synthesis of the Macrocyclic Lactone, Dideoxyzearalane

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Received May 6, 1968

Dideoxyzearalane, 2-(10-hydroxyundecyl)benzoic acid lactone (**2**), the simplest macrocyclic lactone having the same skeletal structure as the macrolide zearalenone (**1**) was totally synthesized. Condensation of 10-undecenoic anhydride with phthalic anhydride gave 3-(9-decenylidene)phthalide (**3**). The internal double bond of diene **3** was in effect reduced in alkali with sodium borohydride and the terminal double bond was hydrated with mercuric acetate and sodium borohydride to yield 3-(9-hydroxydecyl)phthalide (**5**). Saponification and catalytic hydrogenolysis of **5** gave 2-(10-hydroxyundecyl)benzoic acid (**7a**). (±)-Dideoxyzearalane (**2**) was obtained by lactonization of **7a** in benzene at high dilution with phosgene as cyclization agent. Optically active (+) **2** was obtained by hydrogenolysis of **10b**, the dibenzoxazolyl ether of zearalane (**10a**), derived from zearalenone (**1**). This (+) **2** and the totally synthesized (±) **2** are spectroscopically and chromatographically identical.

The structure of the macrolide zearalenone (**1**), the anabolic and uterotropic factor isolated from *Gibberella zeae*,[1] was established in these laboratories.[2] Total syntheses of zearalenone (**1**) and several derivatives have been reported.[3] The subject of this report is the total synthesis of dideoxyzearalane, 2-(10-hydroxyundecyl)benzoic acid lactone (**2**), the simplest macrocyclic lactone having the same skeletal structure as zearalenone (**1**).

The condensation of 10-undecenoic anhydride with phthalic anhydride in the presence of sodium acetate or sodium 10-undecenoate according to the procedure of Mowry, *et al.*,[4] gave 3-(9-decenylidene)phthalide (**3**). Saponification of **3** and reduction with sodium borohydride yielded 3-(9-decenyl)phthalide (**4**).

Markovnikov hydration of the terminal double bond of **4** *via* mercuric acetate addition followed by sodium borohydride demercuration by a modification of the procedure of Brown and Geoghegan[5] gave 3-(9-hydroxydecyl)phthalide (**5**). Alternatively, treatment of **3** with mercuric acetate followed by simultaneous demercuration and reduction in alkali with sodium borohydride yielded **5** directly. The crude product, however, was more complex and less readily purified when prepared in this manner. Hydration of **3** *via* formic acid addition[6] gave primarily the desired secondary alcohol resulting from normal Markovnikov hydration, but also appreciable amounts of other secondary alcohols.

Saponification of **5** yielded the salt of the dihydroxy acid **6** which was converted by catalytic hydrogenolysis[7] of the benzylic hydroxyl group into 2-(10-hydroxyundecyl)benzoic acid (**7a**). Methyl ester **7b** was prepared by reaction of **7a** with diazomethane.

In comparison with the relative ease of cyclization of several related hydroxy acids and esters,[3] the cyclization of hydroxy acid **7a** to lactone **2** proved unexpectedly difficult. Trifluoroacetic anhydride, dicyclohexylcarbodiimide, thionyl chloride, and *p*-toluenesulfonyl chloride all proved unsuitable as lactonization agents. Equally unsuccessful were attempted lactonizations of the hydroxy ester **7b** by transesterification employing aluminum isopropoxide, sodium ethoxide with molecular sieves, sodium triphenylmethoxide, sodium hydride, polymeric dibutyltin oxide, or *p*-toluenesulfonic acid as catalysts. Similar difficulties have recently been reported by Baker, Bycroft, and Roberts[8a] and by Musgrave, Templeton, and Munro[8b] in attempts to prepare di-O-methylcurvularin (**8**) by lactonization of hydroxy acid **9**.

Lactonization of hydroxy acid **7a** to (±)-dideoxyzearalane (**2**) was achieved using phosgene with triethylamine in benzene under high dilution conditions.[9] The major by-product appears to be a polymeric, cyclic ester (see below).

The structure of racemic dideoxyzearalane (**2**) was established by elemental analysis and direct comparison (nmr, ir, uv, and tlc) with an authentic sample of (+)-dideoxyzearalane (**2**). (+)-Dideoxyzearalane (**2**) was prepared by replacement of the phenolic groups of zearalane (**10a**) with hydrogen. This deoxygenation was accomplished by catalytic hydrogenolysis of **10b**, the dibenzoxazolyl ether of **10a**, by a modification of the method of Musliner and Gates.[10] Zearalane (**10a**) was obtained from natural zearalenone (**1**) as previously described.[2]

Hydrolysis of (+)-dideoxyzearalane (**2**) with sodium hydroxide in aqueous dimethyl sulfoxide yielded hy-

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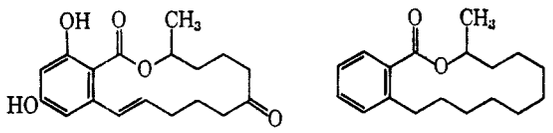

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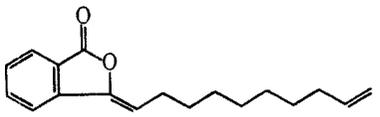

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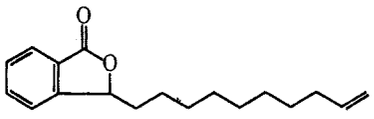

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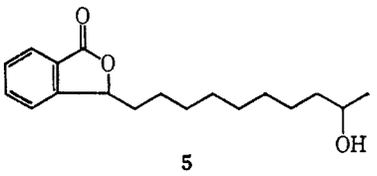

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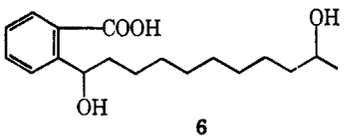

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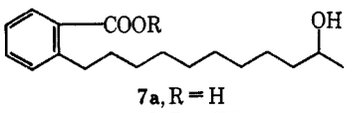
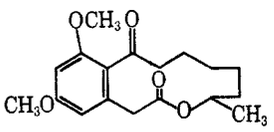


7a, R = H
b, R = CH_3



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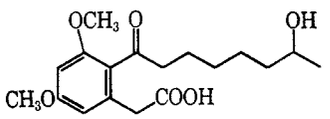

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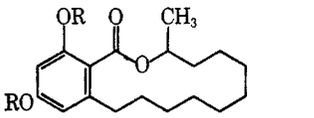
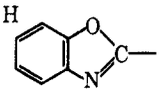


10a, R = H
b, R =



droxy acid (+) **7a** which was converted into methyl ester (+) **7b** with diazomethane. The nmr, ir, and uv spectra and the tlc behavior of these naturally derived products and of the corresponding synthetic compounds were identical.

Lactonization of (+) **7a** with phosgene yielded (+) **2** with complete retention of optical activity through the hydrolysis and relactonization sequence.

The nmr spectrum of dideoxyzearalane (**2**) is characteristically different from the spectra of the open-chain compounds **7a** and **7b**. Replaceable hydrogens are, of course, apparent in the spectra of **7a** and **7b** and absent in the spectrum of **2**. The predictable downfield shift of the multiplet due to the methine hydrogen in **7a** and **7b** (HO—$\overset{|}{\underset{|}{C}}$—H, δ ~3.90 and 3.75 ppm) compared to lactone **2** (RCOO—$\overset{|}{\underset{|}{C}}$—H, δ ~5.35 ppm) is observed. In all cases, the four aromatic hydrogens give a complex pattern of multiplets in the expected 1:3 intensity ratio with the farthest downfield resonance being due to the single hydrogen *ortho* to the carboxyl group. The difference in chemical shift between this *ortho* hydrogen and the chemical shift of the other three hydrogens is considerably less in **2** (ΔHz $\simeq$ 22) than in **7a** (ΔHz $\simeq$ 41) or **7b** (ΔHz $\simeq$ 32). The benzylic hydrogens of the lactone **2** are nonequivalent as clearly shown by their different chemical shifts (δ $\pm$3.3 and 2.7 ppm) and complex splitting patterns. The benzylic hydrogens of the open-chain compounds **7a** and **7b**, however, appear as a crude triplet (δ 3.0 ppm) as expected for nearly equivalent hydrogens on a carbon vicinal to a long methylene group. The nonequivalency of the benzylic hydrogens of dideoxyzearalane (**2**) is probably due to restricted rotation in the sterically crowded lactone.

The nmr spectrum of the major by-product of the lactonization reaction shows no replaceable hydrogens, the methine hydrogen at δ ~5.2 ppm typical of the esters, and patterns for the aromatic and benzylic hydrogens similar to those of the open-chain compounds, suggesting the structure to be a polymeric, cyclic ester or mixture of cyclic esters.

The pharmacological activity of dideoxyzearalane is under study. Application of similar synthetic schemes to the preparation of related products is in progress.

Experimental Section[11]

10-Undecenoic Anhydride.—10-Undecenoic acid (530 g, 2.88 mol) was heated in acetic anhydride (1433 g, 14.0 mol) at reflux for 2.5 hr. Acetic acid and acetic anhydride were removed by distillation at reduced pressure with the pot temperature not exceeding 145°. Molecular distillation of the residue at about 225° (0.05 mm) gave the anhydride (484 g, 96%) as a pale yellow liquid: nmr ($CDCl_3$), δ 5.6 (m, 2, C=C**H**), 4.7 (m, 4, C=CH_2), 2.2 (t, 4, CH_2C=O), 1.9 (m, 4, C=CCH_2), and 1.2 ppm (m, 24, CCH_2C).

Anal. Calcd for $C_{22}H_{38}O_3$: mol wt, 350. Found: equiv wt by titration as an anhydride,[12] 345.

3-(9-Decenylidene)phthalide (3).—The general method of Mowry, *et al.*,[4] for the preparation of alkylidenephthalides was applied to the synthesis of **3**. From 178 g (1.2 mol) of phthalic anhydride and 465 g (1.33 mol) of 10-undecenoic anhydride with 36 g of sodium acetate as catalyst there was obtained 168 g (51%) of **3**: bp 171–183° (0.3 mm); nmr (CCl_4), δ 7.2–8.0 (m, 4, aromatic protons), 5.2–6.2 (m, 2, C=C**H**), 4.6–5.2 (m, 2, C=CH_2), 1.7–2.7 (m, 4, C=CCH_2), and 1.1–1.7 ppm (m, 10, CCH_2C); ir (film), 1770 (C=O), 1680, 1635, 982, and 908 cm^{-1} (olefin); uv max (CH_3OH), 236 mμ (ϵ 17,700), 261 (18,400), 310 (5700).

Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.9; H, 8.20; sapon equiv, 270; iodine no., 188. Found: C, 79.5; H, 8.15; sapon equiv, 270, 273; iodine no., 182, 183.

3-(9-Decenyl)phthalide (4).—A solution of 3-(9-decenylidene)-phthalide (**3**, 54.0 g, 0.2 mol) and sodium hydroxide (200 g, 5 mol) in 50% aqueous tetrahydrofuran (1 l.) was heated at reflux for 3 hr. Sodium borohydride (37.8 g, 1 mol) was then added

(11) Melting points and boiling points are uncorrected. Elemental analyses were performed by Micro-Analysis, Inc., Wilmington, Del., and in our laboratories. Spectra were recorded on the following instruments: uv, Bausch & Lomb Spectronic 505; ir, Perkin-Elmer 21 spectrometer; nmr, Varian Associates A-60A spectrometer (TMS as internal standard); optical activity, O. C. Rudolph and Sons Model 80 polarimeter.

(12) J. B. Johnson and G. L. Funk, *Anal. Chem.*, **27**, 1464 (1955).

to the solution at room temperature. The solution was stirred for 1 hr at room temperature and 1 hr at reflux and cooled to 10°. The cold mixture was poured rapidly into ice-cold 4 *N* hydrochloric acid (2.2 l.) with the temperature not exceeding 25°. The acidic mixture was stirred for 15 min, saturated with salt, and extracted with four 1-l. portions of ether. The dried ($CaSO_4$) extract was concentrated to 100 ml, filtered to remove a small amount of solid, and further concentrated to yield 54.1 g of yellow liquid. Distillation gave 37.7 g (69%) of **4**: bp 146–149° (0.1 mm); nmr ($CDCl_3$), δ 7.2–8.2 (m, 4, aromatic protons), 5.3–6.6 (m, 2, ArCHOC=O and C=CH), 4.7–5.3 (m, 2, C=CH_2), 1.8–3.0 (m, 4, $OCCH_2$ and C=CCH_2), and 0.8–1.8 ppm (m, 12.6, CCH_2C); ir (film), 1760 (C=O), 1635, 992, and 910 cm^{-1} (olefin); uv max (CH_3OH), 228 mμ (ε 10,700), 274 (2300), and 282 (2300).

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.4; H, 8.85; sapon equiv, 272; iodine no., 93.2. Found: C, 79.7; H, 8.90; sapon equiv, 276; iodine no., 94.8.

A second fraction of product (5.8 g, 11%) was also collected: bp 149–165° (0.1 mm); tlc behavior identical with major fraction; iodine no., 92.8.

3-(9-Hydroxydecyl)phthalide (5). A.—Following, in general, the olefin hydration procedure of Brown and Geoghegan,[5] 3-(9-decenyl)phthalide (**4**, 10.9 g, 0.04 mol) in tetrahydrofuran (10 ml) was added at room temperature to a solution of mercuric acetate (12.8 g, 0.04 mol) in 100 ml of water and 30 ml of tetrahydrofuran. The initial orange color faded to a pale yellow within 12 min. The mixture was stirred for 3.5 hr at room temperature, cooled to 15°, basified with sodium hydroxide (6.0 g, 0.15 mol), and stirred for 15 min more. Ethanol (140 ml) was added and the mixture was cooled to 5°. A solution of sodium borohydride (3.78 g, 0.1 mol) in 3 *N* sodium hydroxide solution (200 ml) was added in 5 min and the alkaline mixture was heated for 1 hr at 70–75°. The mixture was chilled and added in 20 min to ice-cold 4 *N* hydrochloric acid (240 ml). The organic solvents were removed at reduced pressure at 60°. The cooled mixture was saturated with salt and extracted with four 150-ml portions of ether. The dried ($CaSO_4$) extract was evaporated at reduced pressure to give 10.8 g of pale yellow liquid: tlc, two components; terminal double-bond hydration 65–70% (by nmr). The hydration procedure was reapplied to this partially hydrated product to yield 10.5 g of yellow oil: tlc, two major components, one minor component; terminal double-bond hydration 85–95% (by nmr). Purification of this product by column chromatography (silica gel, 2% methanol/benzene) gave 1.13 g of recovered 3-(9-decenyl)phthalide (**4**, 10%) and 8.53 g of 3-(9-hydroxydecyl)phthalide (**5**, 80%): tlc, homogeneous; nmr ($CDCl_3$) δ 7.1–8.1 (m, 4, aromatic protons), 5.2–5.8 (m, 1, ArCHOC=O), 3.4–4.2 (m, 1, OCH), and 0.7–3.4 ppm (m, 20 with 1 removable by deuteration, OH, CCH_2C, and $OCCH_3$, the CH_3 doublet is visible, centered at 1.2 ppm, J = 6 Hz); ir (film), 3400 (OH), 1750 (C=O), and 1108 cm^{-1} (CO, secondary alcohol); uv max (CH_3OH), 228 mμ (ε 10,500), 273 (2100), and 280 (1700).

Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.4; H, 9.03. Found: C, 74.4; H, 9.00.

B.—Hydration of 3-(9-decenylidene)phthalide (**3**, 81 g, 0.3 mol) by the above procedure with rehydration of the initial product gave 67.5 g of a five-component (tlc) product mixture. Distillation [bp 213–220° (0.08 mm)] and column chromatography (Florisil, benzene gradually enriched with methanol used as solvent) gave purified **5** (40%): tlc, homogeneous; nmr ($CDCl_3$), δ 6.9–8.1 (m, 4, aromatic protons), 5.1–5.9 (m, 1, ArCHOC=O), 3.3–4.1 (m, 1, OCH), and 0.6–2.7 ppm (m, 19.3 with 0.9 removable by deuteration, OH, CCH_2C, and $OCCH_3$, the CH_3 doublet is visible, centered at 1.2 ppm, J = 6 Hz).

Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.4; H, 9.03; O, 16.5. Found: C, 74.1; H, 9.09; O, 16.9.

2-(10-Hydroxyundecyl)benzoic Acid (7a).—3-(9-Hydroxydecyl)phthalide (**5**, 2.0 g, 0.0069 mol) in tetrahydrofuran (15 ml) and 20% aqueous sodium hydroxide (15 ml) was heated at reflux for 2 hr. The tetrahydrofuran was removed by distillation and the residue was diluted to 100 ml with water and adjusted to a pH of 10.2 with hydrochloric acid. Palladium (0.5 g, 5% Pd/C) was added and the mixture was hydrogenated in a Parr hydrogenator for 12 hr at 75–80° at 50-psi hydrogen pressure.[7] The filtered mixture was extracted with ether. The aqueous solution was acidified with hydrochloric acid, saturated with salt, and extracted with four 100-ml portions of ether. Removal of the ether by evaporation gave 1.74 g (86%) of 2-(10-hydroxyundecyl)benzoic acid (**7a**) as an oil: nmr ($CDCl_3$), δ 7.7–8.2 (m, 1, aromatic proton), 6.9–7.7 (m, 5 with 2 removable by deuteration, aromatic protons, OH, and COOH), 3.5–4.2 (m, 1, OCH), 2.6–3.5 (crude t, 2, $ArCH_2$), and 0.9–2.6 ppm (m, 19, CCH_2C and $OCCH_3$, the CH_3 doublet is visible, centered at 1.2 ppm, J = 6 Hz); ir (film), 3300 (OH) and 1690 cm^{-1} (COOH); uv max (CH_3OH), 230 mμ (ε 6570) and 280 (850).

Anal. Calcd for $C_{18}H_{28}O_3$: C, 74.0; H, 9.65; neut equiv, 292. Found: C, 74.5; H, 9.65; neut equiv, 291.

Methyl 2-(10-hydroxyundecyl)benzoate (7b) was obtained from **7a** (diazomethane) as a neutral oil: tlc, homogeneous; nmr ($CDCl_3$), δ 7.5–8.0 (m, 1, aromatic proton), 6.8–7.5 (m, 3, aromatic protons), 3.2–4.0 (m, 4, OCH and $COOCH_3$), 2.2–3.2 (crude t, 2, $ArCH_2$), 1.7–2.2 (m, 1 removable by deuteration, OH), and 0.60–1.7 ppm (m, 19, CCH_2C and $OCCH_3$, the CH_3 doublet is visible, centered at 1.2 ppm, J = 6 Hz); ir (film), 3350 (OH) and 1715 cm^{-1} (C=O); uv max (CH_3OH) 239 mμ (ε 7440) and 289 (1220).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.5; H, 9.87. Found: C, 74.2; H, 9.81.

O,O-Di-(2-benzoxazolyl)zearalane (10b).—A stirred mixture of zearalane (**10a**,[2] 30.6 g, 0.1 mol), 2-chlorobenzoxazole (34.8 g, 0.23 mol), and potassium carbonate (35.4 g, 0.26 mol) in acetone (400 ml) was heated at reflux for 24 hr. The warm mixture was filtered and the filter cake was washed with acetone. Concentration and cooling of the filtrate gave 45.7 g (85%) of **10b**: mp 120.5–122.5°; nmr ($CDCl_3$), δ 7.0–7.8 (m, 10, aromatic protons), 4.9–5.7 (m, 1, ArCOOCH), 2.2–3.5 (m, 2, $ArCH_2$), and 0.9–2.0 ppm (m, 19.7, CCH_2C and $OCCH_3$).

Anal. Calcd for $C_{32}H_{32}N_2O_6$: C, 71.1; H, 5.97; N, 5.18. Found: C, 71.8; H, 5.76; N, 5.23.

(+)-Dideoxyzearalane (2).—A solution of **10b** (46.1 g, 0.085 mol) in ethanol (450 ml) was reduced in three portions each in the presence of 5 g of 5% Pd/C catalyst. The reductions were carried out in a Parr hydrogenator at 70° at a hydrogen pressure of 50 psi.[13] The filtered reduction mixtures were evaporated (rotary evaporator) to yield 43.5 g of an oil–solid residue. This residue was twice heated with 300 ml *n*-hexane giving 21 g of benzoxazolidone, mp 136–138°. Evaporation of the hexane solution gave 22.5 g of oil. This oil was redissolved in hexane and the hexane solution was washed with 5% sodium hydroxide solution, 3 *N* hydrochloric acid, and water. The solution was then char treated (Darco G-60), filtered, and evaporated to yield 20.8 g (89%) of (+)-dideoxyzearalane (**2**) as a water-white oil: tlc, homogenous; $[\alpha]_{546}^{25}$ +92° (*c* 1, CH_3OH); nmr ($CDCl_3$), δ 7.6–7.8 (m, 1, aromatic proton), 7.0–7.5 (m, 3, aromatic protons), 5.0–5.7 (m, 1, ArCOOCH), 3.0–3.7 (m, 1, ArCH), 2.4–3.0 (m, 1, ArCH), and 0.8–2.1 ppm (m, 19, CCH_2C and $OCCH_3$, the CH_3 doublet is visible, centered at 1.2 ppm, J = 6 Hz); ir (film), 1710 cm^{-1} (C=O); uv max (CH_3OH) 228 mμ (ε 6500) and (960).

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.8; H, 9.55. Found: C, 78.6; H, 9.94.

(+)-2-(10-Hydroxyundecyl)benzoic Acid (7a).—A solution of (+)-dideoxyzearalane (16.2 g, 0.059 mol) in dimethyl sulfoxide (200 ml) and 20% aqueous sodium hydroxide (120 ml) was heated at reflux for 24 hr. Water (200 ml) was added to the cooled mixture. The alkaline solution was extracted with three 200-ml portions of chloroform and acidified with concentrated hydrochloric acid (60 ml). The acidic mixture was extracted with three 200-ml portions of chloroform, and the chloroform extract was washed with water (100 ml). Further purification was achieved by extraction of the hydroxy acid into aqueous sodium bicarbonate solution, reacidification, and reextraction into chloroform. Removal of the solvent gave 15.6 g (90%) of (+) **7a** as a yellow oil: $[\alpha]_{546}^{25}$ +5° (*c* 1, CH_3OH); nmr ($CDCl_3$), δ 8.0–8.2 (m, 1, aromatic proton), 7.0–7.7 (m, 3, aromatic protons), 6.8–7.0 (m, 2, COOH) and COH), 3.5–4.2 (m, 1, OCH), 2.8–3.3 (crude t, 2, $ArCH_2$), and 1.1–2.0 ppm (m, 19, CCH_2C and $OCCH_3$, the CH_3 doublet is visible, centered at 1.2 ppm, J = 6 Hz); ir (film), 3325 (OH) and 1690 cm^{-1} (C=O); uv max (CH_3OH), 230 mμ (ε 7100) and (1400).

Anal. Calcd for $C_{18}H_{28}O_3$: C, 74.0; H, 9.65. Found: C, 73.8; H, 9.66.

Methyl (+)-2-(10-hydroxyundecyl)benzoate (7b) was obtained from (+) **7a** (diazomethane) as a neutral oil: tlc, homogeneous;

(13) This procedure is patterned after that of Musliner and Gates[10] except that ethanol is used as a solvent at a higher temperature than that recommended.

$[\alpha]_{546}^{25}$ +6° (*c* 1, CH_3OH); nmr ($CDCl_3$), δ 7.6–8.0 (m, 1, aromatic proton), 7.0–7.6 (m, 3, aromatic protons), 3.5–4.2 (m, 4, OCH and $COOCH_3$), 2.5–3.5 (crude t, 2, $ArCH_2$), and 0.9–2.5 ppm (m, 20, 1 removable by deuteration, OH, CCH_2C, and $OCCH_3$, the CH_3 doublet is visible, centered at 1.2 ppm, J = 6 Hz); ir (film), 3325 (OH) and 1715 cm^{-1} (C=O); uv max (CH_3OH) 230 mμ (ε 7300) and 1270).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.5; H, 9.87. Found: C, 74.6; H, 9.95.

(+)-Dideoxyzearalane (2) by Cyclization of (+) 7a.—To a cold (8°), stirred solution of (+) **7a** (2.10 g, 0.0072 mol) and triethylamine (1.68 g, 0.017 mol) in benzene (2050 ml) was added 8 ml of phosgene solution (12.5% in benzene). The mixture was stirred at 8° for 2 hr, at room temperature for several days, and at reflux for 43 hr. The reaction mixture was then washed with water and 3 *N* hydrochloric acid, dried (Na_2SO_4), and evaporated finally at high vacuum to yield 2.08 g of an oil. This oil was separated into fractions by column and preparative plate chromatography to yield 0.47 g (24%) of (+)-dideoxyzearalane: $[\alpha]_{546}^{25}$ +90° (*c* 1, CH_3OH); tlc, homogeneous (four solvent systems) and identical with the behavior of the (+)-dideoxyzearalane obtained by hydrogenolysis of **10b**. The nmr, ir, and uv spectra were also all identical with the corresponding spectra of (+)-dideoxyzearalane obtained by hydrogenolysis of **10b**.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.8; H, 9.55. Found: C, 78.8; H, 9.93.

The other major, partially purified, product (0.5 g) had a low R_f on tlc plates and an nmr spectrum resembling that of dideoxyzearalane except in the aromatic and benzylic hydrogen regions as described in the discussion section.

(±)-Dideoxyzearalane (2).—A solution of (±) **7a** (0.9 g, 0.0031 mol), triethylamine (0.72 g, 0.007 mol), and 3.5 ml of phosgene solution (12.5% in benzene), prepared at 8°, was stirred at 8° for 2 hr, at room temperature overnight, and at reflux for 79 hr. The product, isolated as described for recyclized (+)-dideoxyzearalane, was obtained as an oil (0.21 g, 25%) identical in tlc behavior with that of (+)-dideoxyzearalane. The nmr, ir, and uv spectra were also all identical with the corresponding spectra of (+)-dideoxyzearalane.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.8; H, 9.55. Found: C, 78.5; H, 10.0.

Registry No.—2 (+), 17397-59-0; 2 (±), 17397-60-3; **3**, 17393-24-7; **4**, 17393-25-8; **5**, 17414-48-1; **7a**, 17393-26-9; **7a** (+), 17397-61-4; **7b**, 17393-27-0; **7b** (+), 17397-22-7; **10b**, 17393-28-1; 10-undecenoic anhydride, 17393-29-2.

The Synthesis of DL-Zearalenone[1]

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Received May 20, 1968

DL-Zearalenone (1) has been synthesized by a Wittig reaction between (deca-5,9-dion-1-yl)triphenylphosphonium bromide, diethylene ketal (**17**), and ethyl 4,6-dihydroxy-2-formylbenzoate dimethyl ether (**5**), followed by base-catalyzed lactonization of the derived hydroxy ester **21**, and cleavage of protecting groups.

Zearalenone[3,4] (**1**), a metabolite of pathogenic fungi, has been isolated[5,6] from infected corn by groups at Purdue and at the University of Minnesota. Other structurally related resorcylic acid lactones[7-9] are notable for their antifungal and antibiotic activity. Potent steroidlike anabolic and uterotrophic activity ascribed[5] to zearalenone was therefore of particular interest and prompted the synthesis described here. Syntheses of zearalenone and a related substance, curvularin, have also been completed by other groups.[10-12]

Of the three principal approaches to macrolides which have been described, Baeyer–Villiger oxidation[13] of macrocyclic ketones, per acid oxidation[14] of bicyclic enol ethers, and the direct cyclization of hydroxy acids and esters,[15-17] the last is synthetically most direct and was selected in the present case. The synthesis was further divided into the construction of aromatic (**5**) and aliphatic (**17**) portions, to be linked by a Wittig reaction.

The aromatic portion was readily constructed from ethyl *o*-orsellinate diacetate[18] (**2**) by oxidation with chromium trioxide in acetic acid–acetic anhydride to the aldehyde tetraacetate **3**, followed by hydrolysis to the phenolic aldehyde **4**, and methylation to the required ethyl 4,6-dihydroxy-2-formylbenzoate dimethyl ether (**5**) (Scheme I).

The aliphatic part was constructed as follows. Carbethoxylation[19] of 1-hexen-5-one (**6**) with diethyl carbonate and sodium hydride gave the β-keto ester **7**. Michael addition to methyl vinyl ketone then extended the carbon chain to the required length forming the diketo ester **8**. Hydrolysis and decarboxylation of this substance led, not unexpectedly, to a cyclic product **9** rather than the required *n*-decyl derivative **12**. However, basic hydrolysis of the keto ester **8** was achieved by way of the intermediate ketal **10** in which the reactive functions are protected. Decarboxylation and ketal cleavage under acidic conditions then gen-

(1) Presented in part at the 154th National Meeting of the American Chemical Society, Chicago, Ill., 1967, Publication No. 338 from the Syntex Institute of Steroid Chemistry, p 7P. For Publication No. 337, see F. Alvarez, E. Denot, E. Necoechea, J. Calva, P. Crabbé, and A. Bowers, submitted for publication.

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