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PREPARATION AND OPTICAL ROTATORY DISPERSION STUDY OF TETRACYCLIC DITERPENOID INTERMEDIATES[1]

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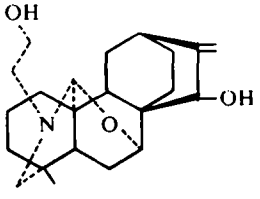
Abstract—As part of a synthetic approach to the diterpenoid alkaloids, ajaconine and atidine, a number of optically active tetracyclic intermediates possessing a carbonyl group at C-7 and a bicyclo[2.2.2.]octane C, D-ring system was obtained. The ORD curves of these compounds provided interesting insight into the effect of C, D ring substituents on the conformation of the B-ring. A pentacyclic unsaturated keto-lactam (**25**), useful for further conversion to ajaconine and atidine, has been synthesized.

WE HAVE previously described an approach to the synthesis of the diterpenoid alkaloids, ajaconine (**1**) and atidine (**2**).[4, 5] * We now wish to report further progress in



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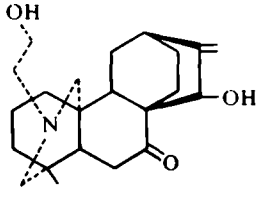

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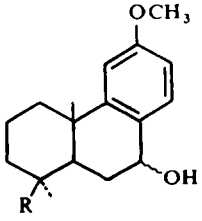
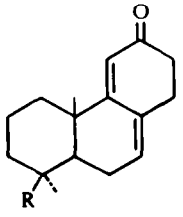
this area. In addition, we wish to report the results of a study of the ORD spectra of the tetracyclic ketones prepared. In the initial synthetic sequence methyl-O-methyl-7-ketopodocarpate, prepared as previously described,[6] was reduced with LAH to give diol **3**, which on Birch reduction and hydrolysis gave crystalline hydroxydienone **4** (yield 57% from **3**). Dienone **4** was reduced with sodium borohydride, acetylated



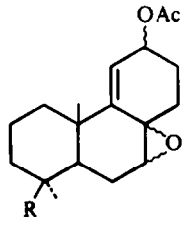
3: R = CH_2OH
14: R = CO_2CH_3



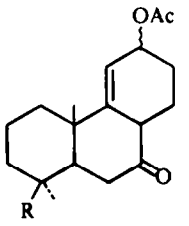
4: R = CH_2OH
15: R = CO_2H
16: R = CO_2CH_3

* The synthetic sequence described would lead to the enantiomers of the diterpenoid alkaloids.

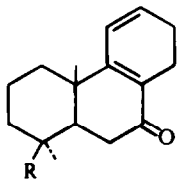
with acetic anhydride in pyridine, and the resulting mixture of epimers was epoxidized with *m*-chloroperbenzoic acid to yield **5** as an amorphous glass which was used without further purification. Treatment of **5** with BF_3 · etherate gave ketone **6** which after chromatography on alumina gave oily dienone **7** (yield 80% from **5**) which could not be crystallized. On treatment with maleic anhydride in refluxing toluene **7** gave



5: R = CH_2OAc
17: R = CO_2CH_3



6: R = CH_2OAc



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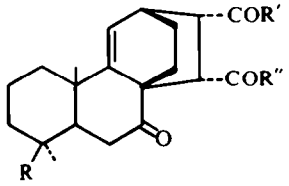
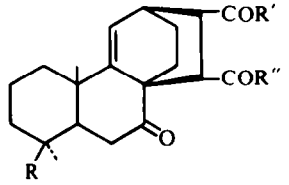
18: R ≅ CO_2CH_3

two crystalline adducts **8** and **9** in 53% yield in a ratio of 3:2 respectively. The adducts were separated by fractional crystallization from chloroform. The presence of a doublet (J = 7 Hz) centred at δ 6·10 in the NMR spectra and a saturated ketone CO



8: R = CH_2OAc, R″ ≡ R′ = 0
10: R = CH_2OAc, R″ = R′ = OCH_3
19: R = CO_2CH_3, R″ = R′ = OCH_3



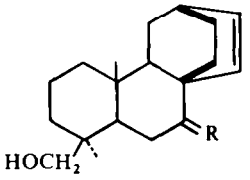
9: R = CH_2OAc, R′ ≡ R″ = 0
11: R = CH_2OAc, R′ = R″ = OCH_3
20: R = CO_2CH_3, R′ = R″ = OCH_3

band at 1709 cm^{-1} in the IR spectra of both adducts indicated that the Diels–Alder reaction had occurred in the anticipated fashion leading to the desired bicyclo[2.2.2] octane C, D-ring system. The relative stereochemistry of addition in the two adducts, however, was still undefined. Evidence for the above stereochemical assignments was obtained on esterification of the two compounds with ethereal diazomethane in methanol. Compound **8** reacted rapidly to yield a diester (**10**) which showed tertiary Me signals at δ 1·02 and 1·12 in its NMR spectrum (*vs* δ 1·01 and 1·18 in the parent anhydride). Compound **9** reacted much more slowly with diazomethane to yield a diester (**11**) which showed tertiary Me signals in its NMR spectrum at δ 1·00 and 1·31 (*vs* one singlet δ 1·02 (6H) in the parent anhydride). The large shift in position of the Me signal on esterification and the apparent steric hindrance to reaction suggest that **9** has its anhydride function positioned in close proximity to the C-10 Me group.* Thus the stereochemistry of the C, D-ring system in **9** was assigned as above.

If we assume that the Diels–Alder reaction has occurred with the formation of only "endo" products as is generally observed,[8] then the stereochemistry of the C,D-ring

* Earlier[4] it was felt that the shift in position of the C-10 Me group observed in the NMR spectrum of **9** might be due to a change in conformation of the B-ring on esterification. However. recent ORD data (Table 2) indicate that no change occurs in the conformation of ring B in going from **9** to **11**.

system in **8** can be assigned as indicated. Further evidence for the assignment of an α-orientation to the ethylene bridge bearing the anhydride moiety in **8** was obtained as follows. Diester **10** (derived from **8**) was saponified with potassium hydroxide in aqueous methanol to yield the corresponding hydroxydiacid which was hydrogenated, acetylated, then oxidatively bisdecarboxylated with lead tetraacetate in pyridine to yield crystalline olefin **12** after saponification of the crude product. Wolff–Kishner reduction of **12** gave olefin **13** identical (IR, NMR, MP) with a known sample.[7]

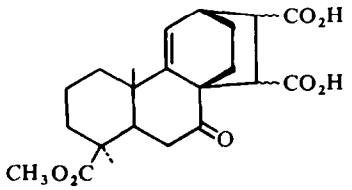


12: R = O H
13: R = < H

Although **12** appeared to be a potential intermediate for the synthesis of ajaconine and atidine, the available quantity was small and considerable difficulty was encountered in oxidation of the C-4 hydroxymethylene group in good yield. With this in mind we set out to alter the synthetic scheme such that the carboxyl group at C-4 present in the starting material might be retained. This was readily accomplished by selective reduction in the initial step. Thus, reduction of methyl-O-methyl-7-ketopodocarpate[6] which sodium borohydride yielded crystalline hydroxyester **14**. Reduction of **14** with sodium in liquid ammonia in the presence of ethanol and THF followed by hydrolysis with hydrochloric acid in methanol gave dienone **15** in 60% overall yield. Compound **15** was treated with ethereal diazomethane to yield the corresponding ester **16**. Reduction of **16** with sodium borohydride, acetylation, and treatment of the epimeric mixture with *m*-chlorperbenzoic acid yielded **17** as an amorphous compound which was used without further purification. After rearrangement of **17** with BF_3 · etherate and chromatography on alumina dienone **18** was obtained as a pure crystalline solid. Reaction of **18** with maleic anhydride in refluxing toluene gave a mixture of anhydride adducts. Esterification of the crude mixture followed by chromatography on alumina gave crystalline triester adducts **19** and **20**. Tentative structure assignments based on spectral data were confirmed for both compounds by correlation with the adducts **8** and **9** obtained earlier. Thus, treatment of **9** with aqueous sodium carbonate, esterification of the hydroxydiacid produced, followed by Kiliani oxidation[9] and further esterification yielded a compound identical in all respects with adduct **20**. Similar treatment of **8** yielded a compound identical with adduct **19**.

The secondary esters of adduct **19** could be selectively hydrolyzed in the presence of the tertiary ester by short treatment with potassium hydroxide in refluxing aqueous methanol leading to **21**.

Compound **21** was hydrogenated using Pt/C catalyst in acetic acid to yield **22**. Oxidative bisdecarboxylation of **22** with lead tetraacetate in pyridine gave crystalline olefin **23**. Saponification of the tertiary ester proceeded smoothly on heating **23** with potassium hydroxide in aqueous diethylene glycol. Reaction of the resulting acid (**24**) with thionyl chloride produced a crystalline acid chloride which was treated



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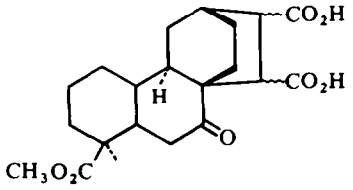

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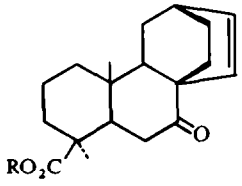
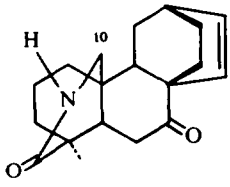
with sodium azide in aqueous dioxane without further purification. Extraction of the acyl azide with hexane and photolysis of this solution followed by chromatography over alumina of the crude product yielded lactam **25** as a pure crystalline solid. This compound was readily differentiated from the other products of the reaction by the presence in its NMR spectrum of only one tertiary Me signal (δ 1·17) assignable to the C-4 Me group. Other products to be expected[10] from the photolysis reaction would possess two Me groups. The protons on C-10 are now part of the lactam bridge and are clearly visible in the NMR spectrum as a doublet of doublets. The presence of the lactam bridge is also supported by the IR spectrum which shows, in addition to the ketone CO band at 1700 cm^{-1}, a lactam CO band at 1650 cm^{-1} and the characteristic N-H absorption at 3200 cm^{-1}. Lactam **25** is a key intermediate for the synthesis of a jaconine and atidine and should be convertible into these alkaloids by previously described procedures.[7,11,12] These transformations will be undertaken when sufficient supplies of **25** become available.



23: R = CH_3, **24**: R = H



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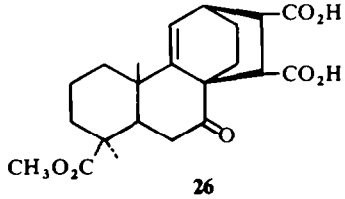
Attention was next turned to transformations of adduct **20**. Hydrolysis of **20** with potassium hydroxide in aqueous methanol gave diacid ester **26** analogous to compound **21**. However, in contrast to **21** which was readily hydrogenated, compound



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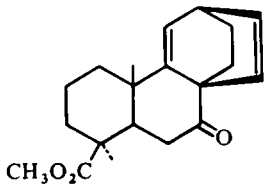
26 could not be hydrogenated even under very severe reaction conditions. It is felt that this resistance to hydrogenation is due to the fact that all of the polar groups in the compound reside on the same face (β) of the molecule and this leads to adsorption on the catalyst surface of the β side, the side remote from the double bond. A similar explanation has been suggested by Pelletier[13] for the difference in adsorption on alumina of epimeric atisine derivatives.

Earlier it had been observed that bisdecarboxylation of compounds analogous to **26** failed to give a diene product.[14,15] It was found, however, that very careful bisdecarboxylation of **26** with lead tetraacetate in pyridine gave diene **27** as a pure crystalline solid (29%). The structure of **27** was supported by its NMR spectrum which showed the C-4 Me signal in the usual position (δ 1·23) while the C-10 Me signal was observed at considerably higher field (δ 0·72) due to the shielding effect of the new double bond. (Preparation of an isomer of **27**. compound **28**, was possible by electrolytic decarboxylation[16,17] of diacid **21**). Compound **27** was selectively hydrogenated using Pd/C catalyst in ethanol to yield **29**. Reduction of **27** using excess hydrogen and



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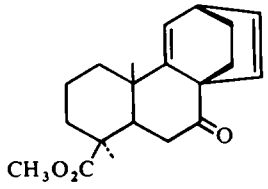

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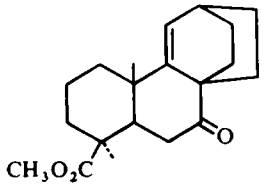

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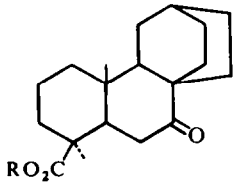
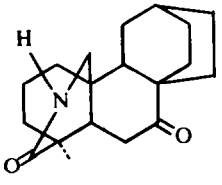
Pt/C catalyst in acetic acid gave ketoester **30** after reoxidation of some C-7 alcohol produced. Saponification of **30** gave acid **31** which was converted to lactam **32** in a manner analogous to the preparation of **25** as described above.



30: R = CH_3
31: R = H



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Some interesting facts concerning the conformation of the B-ring in the above tetracyclic ketones have been revealed by a study of their ORD spectra. The results are summarized in the following Tables.

TABLE 1. ORD RESULTS FOR SATURATED B-RING TETRACYCLIC KETONES

Compound	Amplitude	B-Ring conformation indicated
23	− 95	Chair
24	− 86	Chair
25	− 88	Chair
30	−107	Chair
31	− 90	Chair
32	− 81	Chair
12	− 85	Chair

The compounds shown in Table 1 possess a saturated cyclohexanone B-ring, and all experimentally show a negative Cotton effect. As seen in Fig. 1, the octant rule[18] predicts a negative Cotton effect for these compounds, when their B-rings occupy a chair conformation (the boat form is predicted to show a positive Cotton effect). Thus all of these compounds have their B-rings in a chair conformation. In compounds containing β,γ-unsaturation at C-15, C-16 (**23**, **24**, **25** and **12**) the double bond lies approximately in the plane of the group and apparently makes a negligible contribution.

TABLE 2. ORD RESULTS FOR TETRACYCLIC B-RING KETONES CONTAINING *EXOCYCLIC* β,γ-DOUBLE BONDS

Compound	Amplitude	B-Ring conformation indicated
9	+ 36	boat
11	+ 43	boat
20	+ 46	boat
26	+ 34	boat
29	+ 41	boat
8	− 77	chair-like
10	− 92	chair-like
19	−134	chair-like
27	+ 57	—
28	− 33	—

All compounds in Table 2 have a B-ring which forms part of a β,γ-unsaturated cyclohexanone system. It is known[19] that such systems, having the appropriate geometry, can show intense uv absorption and very strong Cotton effects. However, when the geometry of the system is such that the CO and ethylenic linkages cannot interact properly, the properties of the compound are more reminiscent of a saturated system,[19,20] and the Cotton effects are probably best interpreted in terms of the octant rule[18] for a saturated system. In the case of compounds **8**, **9**, **10**, **11**, **19**, **20**, **26** and **29** the observed Cotton effects are of the same order of magnitude as the Cotton

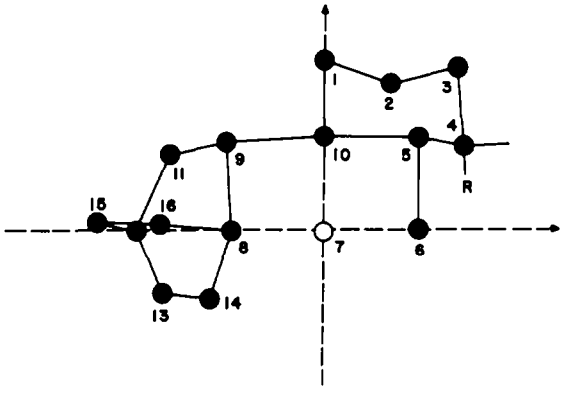

FIG 1. Application of Octant Rule to Compounds in Table 1 with Chair Conformation of B-Ring

effects for the analogous saturated compounds so that application of the octant rule to these compounds appears to be reasonable. This conclusion is further supported by the UV spectra of the compounds which indicate a minimum of interaction between the β, γ-double bond and the CO group.

The observed positive Cotton effects for compounds **9**, **11**, **20**, **26** and **29** are indicative of B-ring boat conformations in these compounds while the negative Cotton effects observed for compounds **8**, **10** and **19** are indicative of chair-like conformations for these compounds (Figs. 2 and 3).

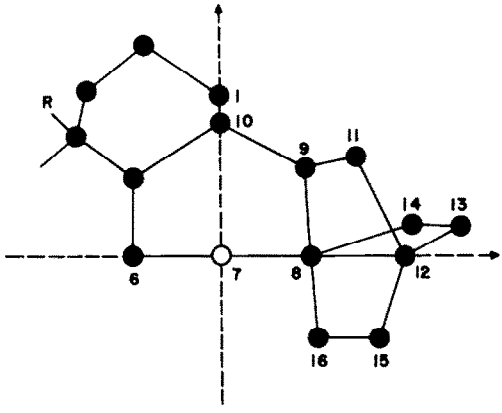

FIG 2. Application of Octant Rule to Compounds in Table 2 with B-Ring Boat Conformation

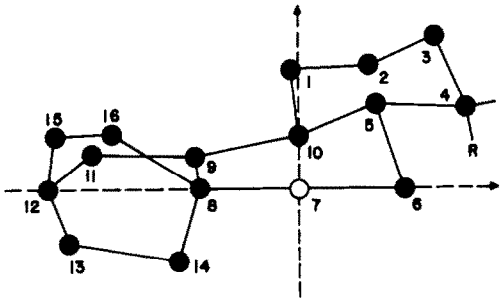

FIG 3. Application of Octant Rule to Compounds in Table 2 with B-Ring Chair-like Conformation

It is interesting to note that the B-rings of the unsaturated compounds (Table 2) undergo a change in conformation on changing substituents on the bicyclic C, D-ring system whereas no such change was observed in the saturated case (Table 1). This is probably a reflection of a lower energy barrier between the boat and chair-like forms of ring B resulting from the introduction of the second sp^2 carbon into the ring. In compounds **9**, **11**, **20**, **26** and **29**, the B-rings prefer to adopt boat conformations presumably in order to relieve the strong diaxial interactions between the bulky C-4 β-groups and the C-6 β-hydrogens. The predominance of the chair-like forms for compounds **8**, **10** and **19** appears to be due to a strong interaction in the alternative boat form, of the bulky α-oriented group at C-16 with the α-hydrogen at C-6.

Compounds **27** and **28** have B-rings which form part of a $\beta\gamma$, $\beta'\gamma'$-unsaturated system. In as much as these compounds show relatively weak Cotton effects it might be assumed that they could be treated as saturated systems. However, we are unable, at this time, to explain the difference in signs of the Cotton effects in **27** and **28**.

EXPERIMENTAL

M.ps were taken on a Thomas–Hoover apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer 237B spectrophotometer with solids in the form of KBr discs and liquids as thin films. NMR spectra were obtained with a Varian A-60 spectrometer using $CDCl_3$ as solvent, except where indicated, and TMS as an internal standard. All mass spectra were obtained using a Varian M-66 mass spectrometer. UV and ORD spectra were recorded using a Jasco ORD/UV-5 instrument. Gas chromatograms were recorded using an F & M Biomedical Gas Chromatograph Model 400 equipped with 6 ft × ¼ in (od) glass columns of the specified coating on Gas Chrom Q. A hydrogen flame detector was employed. Photolyses were performed with a 400 watt Hanovia mercury lamp through a quartz filter. Microanalyses were performed by Alfred Bernhardt Microanalytical Laboratories, Elbach über Engelskirchen, West Germany.

Preparation of dienone **4**. LAH (3 g) was added cautiously to anhyd THF (200 ml) then methyl-O-methyl-7-ketopodocarpate (30 g) dissolved in anhyd THF (100 ml) was added dropwise and the mixture refluxed for 47 hr. Excess LAH was destroyed with wet ether, water (100 ml) was added, and the mixture extracted several times with ether. The ether extracts were combined, dried and concentrated to yield diol **3** (21·7 g) as a viscous, yellow liquid, ν_{max} 3350, 1605, 1570 cm^{-1}.

Sodium metal (40 g) was added slowly to liquid ammonia (1000 ml), then diol **3** (44 g) dissolved in EtOH (400 ml) was added dropwise. The blue color obtained on addition of Na metal persisted throughout the addition of the diol but disappeared shortly thereafter. Water (2000 ml) was then added cautiously to the mixture, the excess ammonia was allowed to evaporate and the mixture extracted several times with ether. The ether extracts were combined, washed with water, dried and concentrated to yield a gummy, yellow material (31·8 g). This material was dissolved in MeOH (200 ml), the pH of the soln was adjusted to a value of 2 with 6N HCl, and the soln allowed to stand at room temp for 5 hr. Water (800 ml) was added, and the soln was extracted with ether. The ether extract was washed with water, dried and concentrated to yield a gummy, yellow solid (28·6 g). On trituration with ether–light petroleum solvent (1:1) dienone **4** was obtained as a crude solid (8·8 g), m.p. 113–118°. The solvent was removed from the mother liquor leaving a gummy residue (20·0 g). This material was dissolved in MeOH (200 ml), Girard's "T" reagent (10 g) was added, the soln was refluxed for 2·5 hr, cooled and poured into 5% $NaHCO_3$aq (1000 ml). Extraction of this mixture with ether yielded the non-ketonic material as a brown, viscous substance (10·0 g). The bicarbonate layer was then acidified with 3N HCl (200 ml), the soln was again extracted with ether, the ether was washed with water, dried and concentrated to yield **4** as a semi-crystalline material (9·6 g). This material on recrystallization from ether gave **4** as well formed prisms, m.p. 131–133°; ν_{max} 3450, 1650, 1630 cm^{-1}; NMR δ 1·02 (3H, s), 1·05 (3H, s), 3·73 (2H, q, J = 11 Hz), 5·83 (1H, s), 6·05 (1H, broad s); UV λ_{max}^{EtOH} 289 mμ (ε = 17,500). (Found: C, 78·36; H, 9·11. $C_{17}H_{24}O_2$ requires: C, 78·46; H, 9·23%).

Preparation of dienone **7**. A soln of $NaBH_4$ (4 g) in water (50 ml) was added to a soln of **4** (12 g) in EtOH (100 ml) and the mixture was stirred overnight. The mixture was then diluted with water (1000 ml) and extracted with ether. The ether layer was washed with water, dried and concentrated to yield the epimeric diols as a gummy liquid (13·3 g), ν_{max} 3350, 1650, 1600 cm^{-1}. This crude diol was dissolved in dry pyridine (75 ml), Ac_2O (11 ml) was added and this mixture was allowed to stir overnight. The mixture was diluted with ether (500 ml), extracted twice with cold water, twice with cold 5% HCl, and again with water. The ether layer was then dried and concentrated to yield the corresponding diacetates as an epimeric mixture, ν_{max} 1730, 1270 cm^{-1}; NMR (CCl_4) δ 0·95 (3H, s), 1·05 (3H, s), 2·00 (6H, s), 4·15 (2H, q, J = 11 Hz), 5·51 (2H, complex).

The above mixture (13·5 g) was dissolved in dry ether (200 ml), and *m*-chloroperbenzoic acid (8 g) in ether was added. The soln was cooled for a few hr then stirred for 18 hr, again cooled, 5% Na_2SO_3aq added until the mixture no longer colored starch iodide paper and the soln was then washed with 3% $NaHCO_3$aq until a sample of the ether soln no longer gave a ppt on addition on HCl. The ether was next washed with cold water, dried and concentrated to yield the epimeric epoxyacetates (**5**) as a viscous yellow liquid (16·1 g), ν_{max} 1740, 1270 cm^{-1}; NMR (CCl_4) δ 1·00 (3H, s), 1·05 (3H, s), 1·75 (3H, s), 1·78 (3H, s), 5·74 (1H, complex).

To a cooled soln of **5** (16·1 g) in dry benzene (100 ml) was added with stirring, a soln of BF_3·etherate (4 ml) in benzene (10 ml). After stirring for 5 min the soln was diluted with water (200 ml), the resulting mixture was extracted with ether, the ether layer was separated, dried and concentrated to yield a yellow oil (16·1 g), ν_{max}^{film} 1748, 1725, 1665, 1260 cm^{-1}. This material was then placed on a column of alumina (acid washed, activity II) prepared in light petroleum. The material was allowed to stand on the column for 2 hr followed by elution with benzene to yield dienone **7** as a light yellow liquid (2·5 g) which resisted crystallization. Further elution with ether gave more of the same compound (6·3 g), ν_{max}^{film} 1740, 1660, 1250 cm^{-1}; NMR (CCl_4) δ 1·00 (3H, s), 1·15 (3H, s), 2·01 (3H, s), 4·16 (2H, q), 6·38 (2H, complex); λ_{max}^{EtOH} 308 mμ (ε = 6,040).

Diels–Alder addition of maleic anhydride to dienone **7**

A soln of **7** (8·8 g), maleic anhydride (9 g) and a trace of trichloroacetic acid in xylene (15 ml) was refluxed for 2 hr. After the mixture was cooled, ether was added whereupon a crystalline solid separated. The solid was collected and fractionally crystallized from chloroform to give adduct **8** (32% yield), m.p. 200–203°; ν_{max} 1835, 1770, 1724, 1709, 1620 cm^{-1}; NMR δ 1·01 (3H, s), 1·18 (3H, s), 2·05 (3H, s), 6·1 (1H, d, J = 7 Hz); λ_{max}^{MeOH} 287 mμ (ε = 45); ORD (*c*, 0·53; MeOH), 25°: $[\phi]_{589}$ −76°; $[\phi]_{313}$ −1244°; $[\phi]_{300}$ ±0°; $[\phi]_{262}$ +6420°; $[\phi]_{246}$ +7200°; a = −76·64. (Found: C, 68·65; H, 7·03. $C_{23}H_{28}O_6$ requires: C, 68·98; H, 7·05%) and adduct **9** (21% yield), m.p. 270–272°; ν_{max} 1852, 1779, 1724, 1709, 1620 cm^{-1}; NMR δ 1·02 (6H, s), 2·08 (3H, s), 6·10 (1H, d, J = 7 Hz); λ_{max}^{MeOH} 285 mμ (ε = 54); ORD (*c*, 0·118; MeOH), 20%: $[\phi]_{589}$ −325; $[\phi]_{302}$ −305°; $[\phi]_{264}$ −3868°; $[\phi]_{242}$ −5600°; a = +35·63. (Found: C, 68·62; H, 6·85. $C_{23}H_{28}O_6$ requires: C, 68·98; H, 7·05%).

Preparation of diester **10**. To a suspension of **8** (100 mg) in MeOH (5 ml) was added excess ethereal diazomethane soln. After stirring for 2 hr the soln was concentrated to yield a white solid which on recrystallization from MeOH gave **10** (90 mg), m.p. 161–163°; ν_{max} 1751, 1739, 1724, 1704 cm^{-1}; NMR δ 1·02 (3H, s), 1·12 (3H, s), 2·06 (3H, s), 3·51 (3H, s), 3·58 (3H, s), 5·93 (1H, d, J = 7 Hz); λ_{max}^{MeOH} 285 mμ (ε = 50); ORD (*c*, 0·127; MeOH), 30°: $[\phi]_{589}$ +281°; $[\phi]_{308}$ −1475°; $[\phi]_{296}$ ±0°; $[\phi]_{260}$ +7740°; $[\phi]_{240}$ +9280°; a = −92.15. (Found: C, 67·50; H, 7·49. $C_{25}H_{34}O_7$ requires: C, 67·32; H, 7·68%).

Preparation of diester **11**. To a suspension of **9** (1·00 g) in MeOH (50 ml) was added excess ethereal diazomethane soln. After stirring for 12 hr the soln was concentrated to yield **11** as a white solid (1·13 g) which on recrystallization from ether gave prismatic crystals, m.p. 178–180°; ν_{max} 1750–1730, 1690, 1620 cm^{-1}; NMR δ 1·00 (3H, s), 1·31 (3H, s), 2·10 (3H, s), 3·53 (3H, s), 3·60 (3H, s), 5·83 (1H, d, J = 7 Hz); λ_{max}^{MeOH} 288 mμ (ε = 101); ORD (*c*, 0·52; MeOH), 25°: $[\phi]_{589}$ −548°; $[\phi]_{300}$ −137°; $[\phi]_{259}$ −4460°; $[\phi]_{240}$ −5760°; a = +43·23. (Found: C, 67·47; H, 7·76. $C_{25}H_{34}O_7$ requires: C, 67·32; H, 7·68%).

Preparation of **12**. A suspension of diester **10** (2·00 g), in a mixture of MeOH (40 ml) and 10% NaOH aq (100 ml) was refluxed under N_2 for 4 hr. After cooling, the soln was diluted with water and extracted with ether extract dried and concentrated to yield a glassy material which on recrystallization from ether–hexane gave the corresponding diacid (1·60 g) as a white solid, m.p. 245–247°; ν_{max} 3450, 1724 cm^{-1}; NMR (CD_3COCD_3) δ 0·97 (3H, s), 1·10 (3H, s), 3·63 (2H, complex), 6·15 (1H, d, J = 7 Hz). This compound (2·20 g) was hydrogenated in the presence of 5% Pt/C catalyst (0·50 g) in AcOH (40 ml). After stirring 48 hr the uptake of one mole of H_2 was complete so the catalyst was removed by filtration and the solvent was evaporated to yield a glassy solid which on recrystallization from ether–pentane gave the saturated compound (2·10 g) as a crystalline solid, m.p. 248–250°; ν_{max} 3380, 1701 and 1748 cm^{-1}. The hydrogenated material (2·32 g) was dissolved in pyridine (5 ml) and Ac_2O (3 ml), the mixture was stirred overnight and then diluted with ether. The ether soln was washed with dil HCl followed by washing with water, drying and concentrating to yield crude acetoxydiacid (2·41 g). This material was dissolved in dry pyridine (30 ml) at 80° under N_2. Lead tetraacetate (1·05 g) was added which resulted in evolution of CO_2. When the bubbling had subsided an additional portion of lead tetraacetate (1·05 g) was added, the mixture reflected 1 hr, the solvent then removed and the residue thoroughly extracted with ether. The ether extract was washed with water, dried and concentrated to yield a crude gum (0·69 g) which was dissolved in a mixture of MeOH (50 ml) and 7% NaOH aq (20 ml). The resulting soln was refluxed 1 hr under N_2, cooled, diluted with water and extracted with ether to yield a semisolid which on recrystallization from ether–light petroleum gave **12** as a white crystalline solid, m.p. 149–150°; ν_{max} 3534, 1689, 1610 and 699 cm^{-1}; NMR δ 0·97 (3H, s), 1·15 (3H, s), 6·28 (1H, complex) and 6·78 (1H, complex); ORD (*c*, 0·17; MeOH), 25°: $[\phi]_{589}$ +85°; $[\phi]_{310}$ −2120°; $[\phi]_{297}$ +0°; $[\phi]_{266}$ +6370; $[\phi]_{238}$ +7640°; a = −84·90. (Found: C, 79·08; H, 9·75. Mol. wt. by mass spectrum 288. $C_{19}H_{28}O_2$ requires: C, 79·12; H, 9·79%. Mol. wt. 288).

Wolff–Kishner reduction of **12**

A soln of **12** (0·097 g), KOH (0·70 g), diethylene glycol (7 ml) and 95% hydrazine (1·5 ml) was refluxed under N_2 for 4 hr, after which water was distilled out. Additional hydrazine (0·5 ml) was then added and the soln refluxed overnight. The mixture was cooled, diluted with water and extracted with ether to yield the crude desoxy compound which on recrystallization from MeOH gave **13** as a crystalline solid (0·089 g), m.p. 148–150° (lit.[8] m.p. 151–152°); ν_{max} 3333, 1618 and 692 cm^{-1}; NMR δ 0·90 (3H, s), 0·91 (3H, s), 3·56 (2H, q, J = 11 Hz) and 6·00 (2H, complex).

Preparation of alcohol **14**. Methyl-O-methyl-7-ketopodocarpate (500 g) was dissolved in THF (700 ml) and 95% EtOH (1000 ml), a soln of $NaBH_4$ (100 g) in water (400 ml) and 95% EtOH (150 ml) was added slowly, and the resulting soln was stirred for 24 hr at RT. A ppt was removed by filtration, the filtrate was concentrated to give a pink syrup, water was added and the resulting mixture was extracted several times with ether (250 ml). The ether extracts were combined, washed twice with brine (200 ml), dried and the solvent evaporated. Recrystallization of the residue from ether gave alcohol **14** (443 g), m.p. 100–106°; ν_{max} 3500, 1715, 1610 and 1575 cm^{-1}; NMR δ 0·87 (3H, s), 1·30 (3H, s), 3·70 (3H, s), 3·81 (3H, s) and 6·81 (3H, complex). (Found: C, 71·88; H, 8·35. Mol. wt. by mass spectrum 318. $C_{19}H_{26}O_4$ requires: C, 71·76; H, 8·24%. Mol. wt. 318).

Birch reduction of alcohol **14**

Preparation of **15**. A soln of **14** (40 g) in THF (100 ml) and abs EtOH (10 ml) was added dropwise over a period of 1 hr to a soln of Na metal (30 g) in liquid ammonia (1000 ml). The soln was stirred for 1 hr, 50% aqueous EtOH (120 ml) was added to discharge the dark blue color, and the excess ammonia was allowed to evaporate. The mixture was diluted with brine (200 ml), extracted several times with ether, and the combined ether extracts were concentrated to give a gummy brown material. This material was dissolved in MeOH (200 ml), conc HCl (10 ml) was added and the resulting soln was allowed to stand overnight at RT. The solvent was evaporated, the residue taken up in ether (300 ml), this soln washed with brine (120 ml), then dried and concentrated to yield a reddish syrup (38 g). The material was dissolved in MeOH (400 ml) and refluxed with Girard's "T" reagent for 3 hr followed by evaporation of the MeOH and distribution of the residue between ether (300 ml) and water (300 ml). The ether layer contained the undesired non-ketonic material. The aqueous layer was acidified with conc HCl (60 ml), allowed to stand on the steam bath for 1 hr and, after cooling to RT, was extracted several times with ether. The combined ether extracts were washed with brine, dried and concentrated to yield crude **15** (24·6 g). Recrystallization from ether gave **15** as a white crystalline solid, m.p. 200–202°; ν_{max} 3500–2500, 1700, 1640, 1575 cm^{-1}; NMR δ 1·03 (3H, s), 1·29 (3H, s), 5·94 (1H, s), 6·15 (1H, broad s), 8·70 (1H, broad s). (Found: C, 74·26; H, 7·99. Mol. wt. by mass spectrum 274. $C_{16}H_{22}O_3$ requires: C, 74·42; H, 8·08%. Mol. wt. 272).

Preparation of dienone **16**. Acid **15** (110 g) was dissolved in MeOH and excess diazomethane was added. After evolution of N_2 had ceased the solvent was removed to yield a viscous residue (112 g) which on recrystallization from ether yielded **16** as white crystals, m.p. 110–111°; ν_{max} 1710, 1650, and 1570 cm^{-1}; NMR δ 0·97 (3H, s), 1·24 (3H, s), 3·73 (3H, s), 5·90 (1H, s) and 6·15 (1H, broad s). (Found: C, 74·77; H, 8·37. Mol. wt. by mass spectrum 288. $C_{18}H_{24}O_3$ requires: C, 74·96; H, 8·39%; Mol. wt. 288).

Preparation of dienone **18**. Dienone **16** (100 g) was dissolved in abs EtOH (700 ml), a soln of $NaBH_4$ (30 g) in water (200 ml) and abs EtOH (50 ml) was added slowly, and the resulting soln was allowed to stand for 20 hr. Removal of the solvent left a yellow residue which was distributed between ether (200 ml) and NaCl aq (200 ml). After separation of the layers the aqueous layer was extracted several additional times with ether (100 ml). The combined ether extracts were washed with water, dried and concentrated to yield the mixture of epimers as a yellow syrup (99 g), ν_{max} 3350, 1700, 1650 and 1600 cm^{-1}.

A soln of the above compound (97·4 g) in dry pyridine (250 ml) and Ac_2O (250 ml) was allowed to stand at RT overnight. After addition of ether (1000 ml), the soln was extracted with water (1000 ml), cold 5% HCl (100 ml) and again with water (1000 ml). The soln was then dried and concentrated to yield the epimeric acetates as a yellow syrup (106 g), ν_{max} 1710, 1600 and 1250 cm^{-1}; NMR δ 0·84 (3H, s), 1·20 (3H, s), 2·08 (3H, s) 3·69 (3H, s) and 5·50 (2H, complex).

The above epimeric mixture (21·3 g) was dissolved in ether (400 ml), the soln stirred at 0°, and *m*-chloroperbenzoic acid (11·26 g) dissolved in dry ether (60 ml) was added. The soln was stirred 1 hr at 0° then overnight at RT. The soln was next treated with 10% Na_2SO aq followed by 4 washings with 4% $NaHCO_3$ aq (100 ml) and finally washed with water, dried and concentrated to give crude **17** (21·0 g), ν_{max} 1720, 1640 cm^{-1}. (Mol. wt. by mass spectrum 348. $C_{20}H_{28}O_5$ requires: Mol. wt. 348).

The crude epoxide (21·9 g) was dissolved in dry benzene (125 ml), the soln stirred at 10°, and BF_3·etherate (4 ml) in dry benzene (10 ml) was added. The soln was stirred for 4·5 min, quenched with water (200 ml), and extracted twice with ether (100 ml). The ether extract was washed with water, dried and concentrated to yield a yellow syrup (20·5 g), ν_{max} 1710, 1650 and 1550 cm^{-1}. This material was dissolved in benzene (20 ml) and adsorbed on an alumina column (350 g), activity II, acid-washed prepared in hexane. The material was allowed to remain on the column for 2 hr then eluted with benzene. Concentration of the benzene eluent gave crude dienone **18** (11·5 g) which on recrystallization from ether gave a white crystalline solid, m.p. 91–92°; ν_{max} 1725, 1650, 1550 cm^{-1}; UV λ_{max}^{hexane}: 296 mμ (ε = 9,100); NMR δ 0·99 (3H, s), 1·27 (3H, s), 3·72 (3H, s), 6·30 (2H, complex). (Found: C, 74·91; H, 8·26. Mol. wt. by mass spectrum 288. $C_{18}H_{24}O_3$ requires: C, 74·96; H, 8·39% Mol. wt. 288).

Preparation of triesters **19** *and* **20**. To a soln of dienone **18** (37·4 g) in xylene (45 ml) was added maleic anhydride (35 g) and a trace of trichloroacetic acid. The mixture was refluxed for 2 hr, cooled and diluted with ether (250 ml), then extracted 8 times with water (500 ml) to remove excess maleic anhydride. The ether layer was dried and concentrated to yield a crude solid (35·4 g) which was dissolved in MeOH (100 ml) and treated with excess ethereal diazomethane. Evaporation of the solvent yielded the crude esters (36 g). This mixture was chromatographed over alumina (2214 g, activity II, acid-washed). Elution with benzene gave adduct **19** (9·8 g) as a crystalline solid, m.p. 151–153°; ν_{max} 1740, 1735, 1720, 1690, 1620 cm^{-1}; NMR δ 0·98 (3H, s), 1·24 (3H, s), 3·46 (3H, s), 3·51 (3H, s), 3·60 (3H, s) and 5·89 (1H, d, J = 7 Hz); λ_{max}^{MeOH} 281 mμ (ε = 34); ORD (*c*, 0·35; MeOH), 30°: $[\phi]_{304}$ −3218°; $[\phi]_{292}$ ± 0°; $[\phi]_{264}$ +10·216°; $[\phi]_{240}$ +11,327°; a = −134·34. (Found: C, 66·84; H, 7·65. Mol. wt. by mass spectrum 432. $C_{24}H_{32}O_7$ requires: C, 66·72; H, 7·47%. Mol. wt. 432) and adduct **20** (7·8 g) as a crystalline solid, m.p. 161–163°, ν_{max} 1745, 1730, 1710, 1700 and 1620 cm^{-1}; NMR δ 1·10 (3H, s), 1·19 (3H, s), 3·43 (3H, s), 3·48 (3H, s), 3·61 (3H, s), 5·80 (1H, d, J = 7 Hz); λ_{max}^{MeOH} 280 mμ (ε = 60); ORD (*c*, 0·35; MeOH), 29°: $[\phi]_{589}$ +197°; $[\phi]_{299}$ +592°, $[\phi]_{289}$ ± 0°; $[\phi]_{242}$ −4210°; $[\phi]_{300}$ −4940°; a = +48·02. (Found: C, 66·59; H, 7·51. Mol. wt. by mass spectrum 432. $C_{24}H_{32}O_7$ requires: C, 66·72; H, 7·47%; Mol. wt. 432).

Saponification of triester **19**

Preparation of **21**. Triester **19** (9·8 g) in MeOH (50 ml) was refluxed for 50 min with NaOH (2·1 g) and water (70 ml). The soln was cooled, diluted with water (250 ml), acidified with dil HCl, and extracted with ether. The ether layer was washed with water, dried and concentrated to give diacid **21** (9·4 g) as a white amorphous compound. ν_{max} 3500–2400, 1725, 1710, 1610 cm^{-1}; NMR (CD_3CO_2D) δ: 0·99 (3H, s), 1·20 (3H, s), 3·69 (3H, s), 6·25 (1H, d, J = 7 Hz), 11·30 (2H, s); ORD (*c*, 0·384; MeOH), 33°; $[\phi]_{304}$ −3365°; $[\phi]_{289}$ ±0°; $[\phi]_{258}$ +6815; $[\phi]_{234}$ +8415; a = −101·8. (Found: C, 65·58; H, 7·07. Mol. wt. by mass spectrum 404. $C_{22}H_{28}O_7$ requires: C, 65·40; H, 6·99%; Mol. wt. 404).

Hydrogenation of compound **21**

Preparation of **22**. Diacid **21** (9·0 g) was dissolved in AcOH (125 ml), 5% Pt/C catalyst (2·3 g) was added, and the soln was stirred under H_2 for 7 days. The catalyst was removed by filtration and the AcOH was evaporated to give a viscous residue (9·0 g) which on recrystallization from MeOH gave **22** as a white solid, m.p. 289–290°; ν_{max} 3500–2400, 1725 and 1705 cm^{-1}; NMR δ 0·84 (3H, s), 1·22 (3H, s), 3·68 (3H, s) and 10·03 (2H, s); ORD (*c*, 0·448; MeOH), 32°; $[\phi]_{305}$ −977°, $[\phi]_{294}$ ± 0°; $[\phi]_{260}$ +4283; $[\phi]_{235}$ +5432°; a = −52·60. (Found: C, 65·00; H, 7·58. Mol. wt. by mass spectrum 406. $C_{22}H_{30}O_7$ requires: C, 65·08; H, 7·45; Mol. wt. 406).

Oxidative decarboxylation of diacid **22**

Preparation of **23**. Diacid **22** was dissolved in dry pyridine (140 ml) at 70° under a N_2. Lead tetraacetate (7 g) was added with stirring and after 10 min an additional portion (3·5 g) was added. After the soln was refluxed for 1·5 hr, the pyridine was evaporated under vacuum, the residue was acidified with dil HCl (150 ml), and this soln was extracted with ether. The ether extract was dried and concentrated to yield a yellow syrup (4·8 g) which was chromatographed on neutral alumina (140 g, activity II). Elution with benzene gave crude **23** which on recrystallization from MeOH gave white crystals, m.p. 108·5–109°; ν_{max} 1725, 1695, 1600 cm^{-1}; NMR δ 1·00 (s, 3H), 1·18 (s, 3H), 3·68 (s, 3H), 6·17 (1H, d of d, J = 7 Hz) and 7·00 (1H, d, J = 7 Hz); ORD (*c*, 0·089; MeOH), 35°: $[\phi]_{308}$ −1280°; $[\phi]_{298}$ ±0°; $[\phi]_{258}$ +8238°; $[\phi]_{222}$ + 14220°; a = − 95·18. (Found: C, 75·84; H, 8·95. Mol. wt. by mass spectrum 316. $C_{20}H_{28}O_3$ requires: C, 76·01; H, 8·92%; Mol. wt. 316).

Saponification of compound **23**

Preparation of **24**. Compound **23** (350 mg), diethylene glycol (13 ml), KOH (1·4 g) and water (0·9 ml) were heated at 165–170° for 4 hr. The soln was cooled, diluted with water (100 ml), made acidic with HCl and extracted with ether. The ether extract was washed with water, dried and concentrated to yield crude acid **24** (300 mg) which on recrystallization from ether yielded **24** as a white solid, m.p. 182–184°; ν_{max} 3600–2400, 1695, 1680 cm^{-1}; NMR δ 1·14 (3H, s), 1·26 (3H, s), 6·28 (1H, d of d, J = 8 Hz) and 6·90 (1H, d, J = 8 Hz); λ_{max}^{MeOH} 281 mμ (ε = 30); ORD (*c*, 0·40; MeOH), 30°: $[\phi]_{589}$ +158°; $[\phi]_{310}$ −1506°; $[\phi]_{299}$ ± 0°; $[\phi]_{263}$ + 7135; $[\phi]_{248}$ + 8003°; a = − 86·41. (Found: C, 75·40; H, 8·48. Mol. wt. by mass spectrum 302. $C_{19}H_{26}O_3$ requires: C, 75·56; H, 8·68%; Mol. wt. 302).

Preparation of lactam **25**. Acid **24** (581 mg) was dissolved in dry ether (75 ml) containing pyridine (0·75 ml) then $SOCl_2$ (7·5 ml) was added, and the soln was allowed to stand for 3 hr. Pyridine hydrochloride was removed by filtration, and the solvent was evaporated to yield the crystalline acid chloride, m.p. 107–110°, γ_{max} 1780, 1700 and 1600 cm^{-1}. The acid chloride was dissolved in dioxane (20 ml) to which sodium azide (1·00 g) and water (8 ml) were added. The soln was shaken vigorously for 8 min then extracted with cold hexane (300 ml). The hexane soln was dried and photolyzed at 0° for 5 hr. Removal of the solvent left a crude product (700 mg) which was chromatographed on alumina (20 g, activity I, acid-washed) to yield in the chloroform–benzene (3:2) eluent crystalline lactam **25** (110 mg), m.p. 253–255°; ν_{max} 3200, 1700, 1650, and 1620 cm^{-1}; NMR δ 1·17 (3H, s), 3·68 (AB system, J = 17 Hz, $\Delta\nu_{AB}$ = 39 Hz) 6·26 (1H, d of d, J = 8 Hz) and 6·98 (1H, d, J = 8 Hz); ORD (*c*, 0·73; MeOH), 31°: $[\phi]_{589}$ +403; $[\phi]_{310}$ −3160°, $[\phi]_{292}$ ± 0°; $[\phi]_{260}$ + 5670°; $[\phi]_{210}$ + 6900°; a = −88·30. (Found: Mol. wt. by mass spectrum 299·1860. $C_{19}H_{25}O_2N$ requires: Mol. wt. 299·1885).

Preparation of diacid **26**. Triester **20** (1·20 g) was dissolved in MeOH (13 ml), and NaOHaq (0·6 g in 16 ml) was added. The soln was refluxed for 2·5 hr, cooled, diluted with water (200 ml), then acidified with 6N HCl and extracted with ether. The ether extract was dried and concentrated to yield **26** as a viscous material (1·10 g) which on crystallization gave a white solid, m.p. 235–236°; ν_{max} 3350–2600, 1728, 1712–1695, 1625 cm^{-1}; NMR δ 0·97 (3H, s), 1·20 (3H, s), 3·70 (3H, s), 6·22 (1H, d, J = 7 Hz), 10·95 (2H, broad s); λ_{max}^{MeOH} 281 mμ (ε = 30); ORD (*c*, 0·145; MeOH) 25°: $[\phi]_{589}$ +83·5°, $[\phi]_{297}$ +2539°, $[\phi]_{275}$ ± 0°, $[\phi]_{257}$ −864°, $[\phi]_{227}$ + 2539°, a = + 34·03. (Found: Mol. wt. by mass spectrum 404; $C_{22}H_{28}O_7$ requires: Mol. wt. 404).

Oxidative decarboxylation of **26**

Preparation of **27**. Diacid **26** (500 mg) was dissolved in dry pyridine (10 ml), the soln flushed for 10 min with O_2, then lead tetraacetate (1 g) added and the flask immersed in a bath at 70 ± 2°. When the vigorous bubbling ceased (20 min), the mixture was poured into 6N HNO_3 (50 ml) and this soln extracted with ether. The ether layer was washed with 10% NaOHaq (200 ml), with water, dried and concentrated to yield a yellow, viscous substance (150 mg), which was passed through a column of neutral alumina (10 g, activity I) eluting with benzene. On concentration of the benzene fractions **27** was obtained as a solid (115 mg) which on recrystallization from ether gave colorless plates, m.p. 105–106°; ν_{max} 1720, 1695, 1625, 1585 cm^{-1}; NMR δ 0·72 (3H, s), 1·23 (3H, s), 3·74 (3H, s), 5·96 (1H, d, J = 6 Hz), 6·47 (2H, complex); ORD (*c*, 0·31; MeOH), 35°: $[\phi]_{306}$ + 3078°, $[\phi]_{288}$ ± 0°, $[\phi]_{272}$ −2614°, $[\phi]_{259}$ −1404°, a = + 56·92. (Found: C, 76·37; H, 8·29. Mol. wt. by mass spectrum 314. $C_{20}H_{26}O_3$ requires: C, 76·50; H, 8·34; Mol. wt. 314).

Selective hydrogenation of compound **27**. *Preparation of* **29**. Diene **27** (273 mg) was dissolved in EtOH (10 ml), 10% Pd/C catalyst (20 mg) was added, and the soln was stirred under H_2 at atmc press for 16 hr. At this time one mole of H_2 had been absorbed. The catalyst was removed and the solvent was evaporated to yield **29** as a viscous material (274 mg) which crystallized on standing, m.p. 89–92°; ν_{max} 1725, 1700, 1625 cm^{-1}; NMR δ 0·85 (3H, s), 1·20 (3H, s), 3·68 (3H, s), 6·02 (1H, d, J = 7 Hz); ORD (*c*, 0·107, Me_3OH) 35°: $[\phi]_{589}$ + 103°, $[\phi]_{307}$ + 2300°, $[\phi]_{288}$ ± 0°, $[\phi]_{270}$ − 1770°, a = + 40·70. (Found: Mol. wt. by mass spectrum 316. $C_{20}H_{28}O_3$ requires: Mol. wt. 316).

Preparation of compound **30**. Compound **29** (264 mg) was dissolved in abs EtOH (10 ml), 5% Pt/C catalyst (100 mg) was added and the soln stirred in a H_2 atme for 48 hr. The catalyst was removed by filtration and the solvent was evaporated to yield a viscous, yellow liquid; ν_{max} 3400, 1725 cm^{-1}. This crude material was dissolved in acetone (50 ml) and Jones Reagent was added dropwise until a yellow color persisted. The excess reagent was destroyed with isopropanol, $NaHCO_3$ was added to neutralize the excess acid, the mixture was centrifuged, and the supernatant was concentrated to yield **30** as a viscous material (260 mg) which crystallized on standing, m.p. 108–110°; ν_{max} 1725, 1695 cm^{-1}; NMR δ 0·93 (3H, s), 1·27 (3H, s), 3·65 (3H, s); ORD (*c*, 0·13; MeOH) 27°: $[\phi]_{589}$ +171°, $[\phi]_{310}$ −2910, $[\phi]_{298}$ ± 0°, $[\phi]_{268}$ +7791°,

a = −107·01. (Found: C, 75·63; H, 9·40. Mol. wt. by mass spectrum 318. $C_{20}H_{30}O_3$ requires: C, 75·47; H, 9·43% Mol. wt. 318).

Preparation of compound **31**. Compound **30** (248 mg) was mixed with diethylene glycol (10 ml) and water (0·6 ml), then KOH (1·4 g) was added. The mixture was heated under a N_2 atm at 160–170° for 4 hr, cooled, diluted with water (100 ml), acidified with 6N HCl, then extracted with ether. The ether was washed with water, dried and evaporated to yield **31** (212 mg) as a brown gum which on recrystallization from ether gave a white solid, m.p. 176–179°; ν_{max} 3400–2600, 1730–1700, 1690–1670 cm^{-1}; NMR δ 1·05 (3H, s), 1·20 (3H, s), 9·72 (1H, s, broad s); ORD (*c*, 0·485; Me_3OH) 27°: $[\phi]_{589}$ +754°, $[\phi]_{311}$ −2480°, $[\phi]_{298}$ ± 0°, $[\phi]_{267}$ +6540°, $[\phi]_{236}$ +7540°, a = −90·20. (Found: C, 75·00; H, 9·40. Mol. wt. by mass spectrum 304. $C_{19}H_{28}O_3$ requires: C, 75·00; H, 9·21% Mol. wt. 304).

Preparation of lactam **32**. Acid **31** (624 mg) was dissolved in dry ether (25 ml) containing pyridine (2 drops), then $SOCl_2$ (25 ml) was added with stirring. After 3 hr, the soln was filtered and the filtrate concentrated to yield the acid chloride as a brown residue which crystallized in part, ν_{max} 1790, 1690 cm^{-1}. The crude acid chloride was dissolved in dry dioxane (20 ml), a soln of sodium azide (1 g) in water (8 ml) was added, and the mixture shaken for about 8 min, then extracted with hexane (300 ml). The hexane soln (ν_{max} 2150, 1700 cm^{-1}), after drying over Na_2SO_4, was transferred to the photolysis apparatus and the soln was photolyzed for 5·5 hr at −10°. Evaporation of the solvent gave the crude product (600 mg) which was chromatographed over alumina (activity II, 20 g) eluting with chloroform-benzene solvent. Concentration of the chloroform–benzene (1:1) fractions gave lactam **32** (60 mg) as a crystalline solid, m.p. 248–250°; ν_{max} 3275, 3200, 1690, 1660 cm^{-1}; NMR δ 1·07 (3H, s), 2·38 (2H, d, J = 9 Hz), 3·65 (2H, q, J = 13 Hz); ORD (*c*, 0·407; MeOH) 25°: $[\phi]_{311}$ −2218°, $[\phi]_{297}$ ± 0°, $[\phi]_{270}$ + 5916°, $[\phi]_{246}$ + 4141°, a = − 81·35. (Found: Mol. wt. by mass spectrum 301·2070. $C_{19}H_{27}NO_2$ requires: Mol. wt. 301·2041).

Conversion of adduct **9** *to triester* **20**

Adduct **9** (5·1 g) was dissolved in MeOH (300 ml). 10% Na_2CO_3 aq (60 ml) added and the resulting soln refluxed for 4 hr. The mixture was then cooled, the MeOH evaporated, water (200 ml) added, the soln neutralized with HCl and extracted with ether to yield a colorless, viscous material (5·5 g) which was dissolved in MeOH (100 ml), and excess diazomethane in ether was added. After evolution of N_2 had ceased the solvent was removed to yield the hydroxydiester as a colorless syrup (5·3 g). ν_{max} 3400, 1740, 1695, 1620 cm^{-1}; NMR δ 0·98 (3H, s), 1·10 (3H, s), 3·50 (3H, s), 3·57 (3H, s), 5·83 (1H, d, J = 7 Hz). The hydroxydiester was dissolved in cold AcOH (540 ml). Kiliani's reagent[10] (38 ml) was added dropwise and the soln allowed to stir at RT for 23 hr. The mixture was then poured into brine (1000 ml) and extracted with chloroform. The chloroform layer was then extracted with 5% NaOH aq (100 ml), the basic layer separated, acidified with HCl, and extracted again with chloroform. The chloroform layer was dried and concentrated to yield a viscous substance (ν_{max} 3300–2600, 1730, 1700 and 1620 cm^{-1}) which was dissolved in MeOH (100 ml) and treated with excess diazomethane in ether. When the evolution of N_2 had ceased the solvent was removed to yield a viscous, yellow liquid (3·9 g) which on recrystallization from ether gave a solid identical in all respects with triester **20**.

Conversion of adduct **8** *to triester* **19**

Adduct **8** (262 mg) was dissolved in MeOH (20 ml), 10% Na_2CO_3 aq (4 ml) was added and the resulting soln was refluxed for 4 hr. The mixture was then cooled, the MeOH evaporated, water (100 ml) added, the soln neutralized with HCl and extracted with ether to yield the hydroxydiacid as a syrup (244 mg). ν_{max} 3600–3100, 1725, 1700, 1600 cm^{-1}; NMR δ 1·00 (3H, s) 1·10 (3H, s), 5·38 (1H, broad s), 5·93 (1H, d, J = 7 Hz). Esterification with ethereal diazomethane yielded the corresponding hydroxydiester (250 mg) which was stirred with chromic anhydride (0·3 g) in pyridine (5 ml) at RT for 18 hr. The soln was then filtered, diluted with water (50 ml) and extracted with ether. The ether extract was washed with dil HCl, washed with water, dried and concentrated to yield a glassy material (200 mg). The material was dissolved in ether (100 ml), extracted with 10% NaOH aq (20 ml), the basic layer neutralized with HCl and then extracted with ether (300 ml). The ether extract was washed with water, dried and concentrated to yield a viscous material (30 mg) which was esterified with ethereal diazomethane to yield a substance identical (IR, NMR, GLC) with triester **19**.

Preparation of diene **28**. Diacid **22** (1 g) was dissolved in pyridine (40 ml) and Et_3N (1·25 ml) and water (10 ml) were added and the soln was electrolyzed[17, 18] at ~ 100 volts (0·5–0·8 amps) for 20 min. The mixture was poured into ether, the ether layer extracted with 5% NaOH aq, washed with water, dried and concentrated to give a yellow syrup (380 mg) which gave, after preparative TLC, diene **28** (17 mg), m.p. 86–87°;

ν_{max} 1720, 1690, 1630, 1580 cm^{-1}; NMR δ 0·93 (3H, s), 1·21 (3H, s), 3·69 (3H, s), 4·20 (3H, complex); ORD (*c*, 0·40; MeOH), 26°: $[\phi]_{589}$ +235°; $[\phi]_{355}$ +785°; $[\phi]_{306}$ −471°; $[\phi]_{298}$ ±0° $[\phi]_{248}$ +3689°; $[\phi]_{235}$ +7536°; a = −41·60. (Found: C, 76·30; H, 8·11. Mol. wt. by mass spectrum 314. $C_{20}H_{26}O_3$ requires: C, 76·43; H, 8·28%. Mol. wt. 314).

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