# Terpenoids. Part 39.[1] Total Synthesis of Gibberellins $A_{15}$ and $A_{37}$

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The total synthesis of gibberllins $A_{15}$ (2) and $A_{37}$ (3), in which *ent*-3β,20-epoxy-3-methoxy-16α-tetrahydropyran-2-yloxy-17-norkauran-6α-ol (4) was an important intermediate, is reported.

AFTER our recent completion of the total synthesis [2] of the tumour inhibitor [3] enmein (1), we decided to attempt the syntheses of gibberellins $A_{15}$ ($GA_{15}$)(2) and $A_{37}$ ($GA_{37}$)(3). The structure of $GA_{15}$ was determined by Hanson,[4] and its first total synthesis was accomplished by Nagata *et al.*[5] In the same year, the chemical conversion of enmein (1) into $GA_{15}$ was reported by Somei and Okamoto.[6] We have now synthesised $GA_{15}$ *via* a different route. Gibberellin $A_{37}$ (3β-hydroxy-$GA_{15}$) was isolated as a glucosyl ester from mature seeds of *Phaseolus vulgaris* and characterised by Takahashi *et al.*[7] It was derived from $GA_{36}$ by reduction with sodium borohydride by MacMillan *et al.*[8] Its biological activity has also been reported.[9] Recently, MacMillan *et al.*[10] published a partial synthesis of $GA_{37}$ from $GA_{13}$. A total synthesis of $GA_{37}$, however, has not been described hitherto. This paper provides a full account [11] of the syntheses of the methyl esters of $GA_{15}$ and $GA_{37}$ and of their demethylation to $GA_{15}$ and $GA_{37}$. We investigated in detail two routes: (i) from *ent*-3β,20-epoxy-3-methoxy-16α-tetrahydropyran-2-yloxy-17-norkauran-6α-ol (4) [2] *via* methyl *ent*-3β,20-epoxy-3,16α-dimethoxy-7-oxo-17-norgibberellan-19-oate (6) and (ii) from methyl *ent*-6,20-epoxy-3,3-ethylenedioxy-16α-hydroxy-6-oxo-6,7-seco-17-norkauran-7-oate (5) [12] *via* (6) (Scheme 1).

[1] Part 38, M. Node, H. Hori, and E. Fujita, *J.C.S. Perkin I*, 1976, 2144.

[2] E. Fujita, M. Shibuya, S. Nakamura, Y. Okada, and T. Fujita, *J.C.S. Perkin I*, 1974, 165.

[3] E. Fujita, Y. Nagao, M. Node, K. Kaneko, S. Nakazawa, and H. Kuroda, *Experientia*, 1976, **32**, 203; E. Fujita, Y. Nagao, K. Kaneko, S. Nakazawa, and H. Kuroda, *Chem. and Pharm. Bull.* (*Japan*), 1976, **24**, 2118.

[4] J. R. Hanson, *Tetrahedron*, 1967, **23**, 733.

[5] W. Nagata, T. Wakabayashi, M. Narisada, Y. Hayase, and S. Kamata, *J. Amer. Chem. Soc.*, 1970, **92**, 3202; 1971, **93**, 5740.

[6] M. Somei and T. Okamoto, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 2135; *Yakugaku Zasshi* (*J. Pharm. Soc. Japan*), 1972, **92**, 397.

[7] K. Hiraga, T. Yokota, N. Murofushi, and N. Takahashi, *Agric. and Biol. Chem.* (*Japan*), 1972, **36**, 345; 1974, **38**, 2511.

[8] J. R. Bearder and J. MacMillan, *Agric. and Biol. Chem.* (*Japan*), 1972, **36**, 342; *J.C.S. Perkin I*, 1973, 2824.

[9] K. Hiraga, H. Yamane, and N. Takahashi, *Phytochemistry*, 1974, **13**, 2371.

[10] D. H. Bowen, C. Cloke, D. M. Harrison, and J. MacMillan, *J.C.S. Perkin I*, 1975, 83.

[11] Preliminary report, M. Node, H. Hori, and E. Fujita, *J.C.S. Chem. Comm.*, 1975, 898.

[12] M. Shibuya and E. Fujita, *J.C.S. Perkin I*, 1974, 178.

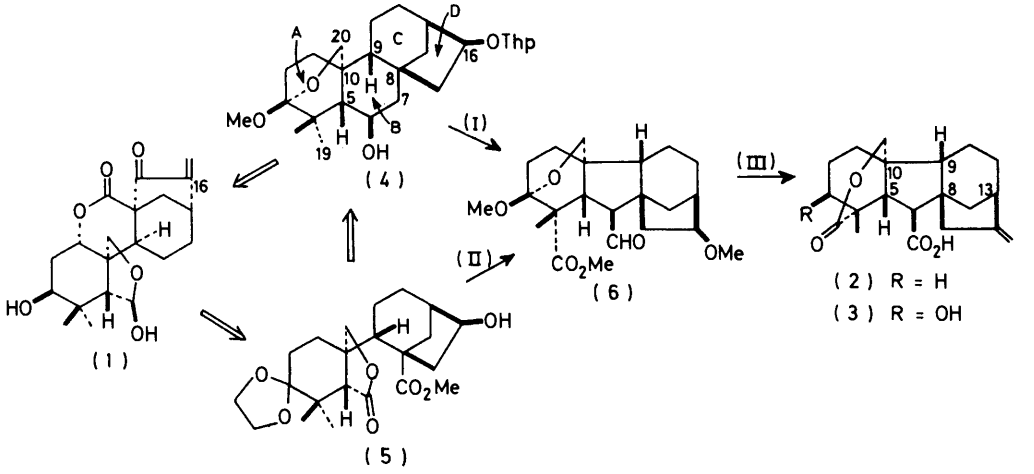
(I) *Synthesis of the Ester* (6) *from the Alcohol* (4).—Compound (4) has been synthesised from naphthalene-1,6-diol *via* 5-methoxy-2-tetralone.[2] Thus the conversion of (4) into the desired compounds would constitute their total synthesis. Compound (4) can also be derived relatively easily from enmein (1), and has the same stereochemistry as $GA_{15}$ and $GA_{37}$ at C-5, -8, -9, -10, and -13. In the total synthesis of enmein (1) the exocyclic methylene group at C-16 was introduced at a late stage; its earlier introduction seemed unwise because of its sensitivity to several reagents. In the present synthesis also it was introduced near the end; before this the presence of a 16β-methoxy group was maintained. Since aliphatic methyl ethers are stable under acidic and basic conditions, *O*-methylation seems suitable for protection of alcohols. However de-*O*-methylation is not always easy, and *O*-methylation has not often been used for this purpose. We investigated the demethylation of several methyl ethers and found a good method involving use of a thiol and boron trifluoride–ether under mild conditions.[13] Protection of all 16-hydroxy-groups by *O*-methylation is a characteristic of the present synthesis.

In the conversion (4) ⟶ (6), oxidation of the 19-methyl group and contraction of ring B were required. We investigated the use of the hypoiodite reaction[14] with many *ent*-16-methoxy-17-norkaurane derivatives in detail, and achieved oxidation in high yield at C-19 in *ent*-3β,20-epoxy-3,16α-dimethoxy-17-norkauran-6α-ol (7) and its 7α-acetoxy-derivative (8), in which the ring A is fixed in the boat form.[15] Ring B contraction for the conversion of kaurane-type into gibberellane-type compounds was also investigated in detail with several derivatives containing the skeleton (9). Treatment of *ent*-3β,20-epoxy-7β-mesyloxy-3,16α-dimethoxy-17-norkauran-19,6β-olide (10) with potassium hydroxide in aqueous t-butyl alcohol and esterification of the product yielded compound (6) quantitatively.[1]

[13] M. Node, H. Hori, and E. Fujita, *J.C.S. Perkin 1*, 1976, 2237.

[14] K. Heusler and J. Kalvoda, *Angew. Chem.*, 1964, **76**, 518; *Synthesis*, 1971, 501.

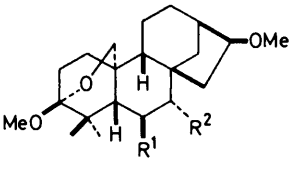
The hypoiodite reaction with compound (4) proceeded as smoothly as with compound (7) and afforded the 19,-6β-olide (11) in 59.4% yield. Acidic hydrolysis gave the 16-ol (67%), which on treatment with diazomethane in the presence of boron trifluoride–ether[16] gave the 16-methoxy-derivative (12)[15] in 48% yield.



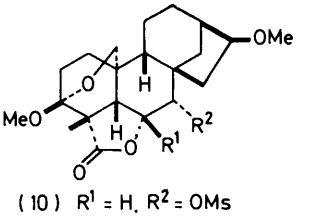

(2) R = H
(3) R = OH

SCHEME 1

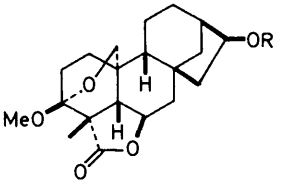
Compound (12) can also be synthesised from (5) in another way [see section (II)]. In order to convert the lactone (12) into (10), which is the most suitable material for ring B contraction, inversion of the configuration at C-6 and introduction of an oxygen function at C-7 were necessary. The lactone (12) was treated with sulphuric acid in absolute methanol to give the methyl ester (13). Dehydration was tried in the hope that a 6,7-double bond would be formed. However, treatment



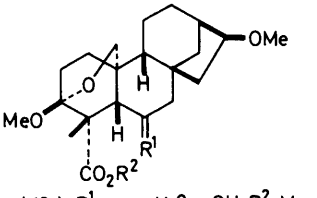
(7) $R^1$ = OH, $R^2$ = H
(8) $R^1$ = OH, $R^2$ = OAc
(9) $R^1$ = $R^2$ = H



(10) $R^1$ = H, $R^2$ = OMs
(14) $R^1$ = $R^2$ = H
(15a) $R^1$ = OH, $R^2$ = H



(11) R = Thp
(12) R = Me

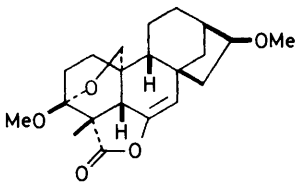


(13) $R^1$ = α—H,β—OH, $R^2$=Me
(15b) $R^1$ = O, $R^2$ = H
(16) $R^1$ = α—H,β—OH, $R^2$ = H

[15] M. Node, H. Hori, and E. Fujita, *Chem. and Pharm. Bull. (Japan)*, 1976, **24**, 2149.

[16] E. Müller and W. Rundel, *Angew. Chem.*, 1958, **70**, 105; E. Müller, M. Bauer, and W. Rundel, *Z. Naturforsch.*, 1959, **14B**, 209.

with phosphoryl chloride in pyridine caused an intramolecular substitution to yield only the 6α-lactone (14). We then studied the conversion of the lactone (12) into (15a). The 6α-lactone system in (14) is very stable. The free hydroxy-carboxylic acid cannot be isolated after hydrolysis, because re-lactonisation takes place



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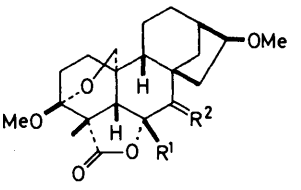
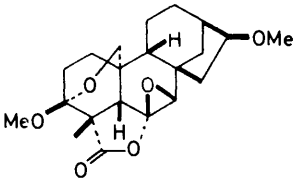


(19a) $R^1$ = OH, $R^2$ = α—H,β—OH
(19b) $R^1$ = F, $R^2$ = α—H,β—OH
(19c) $R^1$ = OMe, $R^2$ = α—H,β—OH
(19d) $R^1$ = OMe, $R^2$ = α—OH,β—H
(20) $R^1$ = H, $R^2$ = α—H,β—OH
(21) $R^1$ = H, $R^2$ = O
(22) $R^1$ = H, $R^2$ = α—OH,β—H



(18)

very easily. Hence, the 6-oxo-19-oic acid (15b) was also expected to form the lactone (15a) very easily. Hydrolysis of the γ-lactone system in (12) with aqueous perchloric acid gave the hydroxy-carboxylic acid (16) in 95% yield, and Jones oxidation of (16) afforded a mixture which consisted almost entirely of (15a), with little (15b), isomer of (17) would be energetically disfavoured because of strain.

Compound (17) on epoxidation by Anderson's procedure [17] gave the epoxide (18) quantitatively, which on treatment with boron trifluoride–ether in wet benzene yielded the diol (19a). The configuration of the epoxide ring in (18) was assigned on the basis of attack of the reagent from the less hindered side, and confirmed as β as follows. When the epoxide (18) was treated with aged boron trifluoride–etherate in dichloromethane, the diol (19a) and the fluoro-alcohol (19b) were obtained. In the reaction of (18) with the same reagent in dichloromethane containing methanol, the methoxy-alcohol (19c) and the fluoro-alcohol (19b) were formed.[1] The i.r. spectra of (19b) and (19c) suggested the presence of a γ-lactone system in each. The formation of secondary alcohols in the ring opening of the epoxide was elucidated by formation of the acetates, the n.m.r. spectra of which showed a doublet (*J* 12 Hz), split by coupling with fluorine, at δ 5.44 for (19b) acetate and a singlet at δ 5.48 for (19c) acetate, assignable C(7)*H*·OAc. Thus the ring opening must have taken place at C-6, producing 7-ols with retention of the original stereochemistry. The introduction of a fluorine atom and a methoxy-group at C-6 in (19b) and (19c), respectively, was supported by analysis and n.m.r. data. The *pro-R* proton at C-20 in (19d),[1] the 7-epimer derived from (19c), resonated at much lower field than that in (19c). This observation suggested a stereochemistry of (19d) in which the 7-

TABLE 1

Chemical shift of the 20-*pro-R*-protons in compound (19) and related compounds [a,b]

| (19a) | (19b) | (19c) | (19a) Acetate | (19b) acetate | (19c) acetate | (12) | (14) | (19d) |
|---|---|---|---|---|---|---|---|---|
| 3.6—4.3 [c] | 4.23 | 4.32 | 4.23 | 4.32 | 4.40 | 4.58 | 4.46 | 4.96 |

[a] δ Values; $Me_4Si$ as internal standard. [b] In the n.m.r. spectrum of compound (26),[15] two doublets of doublets (*J* 10 and 3 Hz; *J* 10 and 1 Hz) were observed at δ 4.87 and 3.86 respectively. The former was reasonably assigned to 20-*pro-R*-H ($H_a$) and the latter to 20-*pro-S*-H ($H_b$). The proton $H_a$ showed long-range coupling with the 1β-H and $H_b$ with the 5β-H. All the signals in this Table were observed as doublets of doublets (*J* 10 and 3 Hz). [c] Overlapped with other signals.

as expected. Dehydration of (15a) with thionyl chloride in pyridine gave the enol lactone (17) in high yield.* In the n.m.r. spectrum of (17), a doublet due to 7-H split by allylic coupling (*J* 3 Hz) was observed, which indicated that selective 6,7-dehydration had occurred, In the synthesis of enmein (1), similar dehydration of compound (4) gave the $\Delta^5$- and $\Delta^6$-products in the ratio 1 : 2.[2] The reason for the formation of only the $\Delta^6$-product (17) in the case of (15a) may be attributable to the following factors. Ring B in structure (4) has a chair form, in which the 6β-hydroxy group has the equatorial conformation. However ring B in (15a) has a twist-boat form [1] because of the presence of a 19,6α-lactone ring; hence the 6β-hydroxy-group has a quasi-axial conformation, *i.e.* stereochemistry favourable for *trans*-elimination with the 7α-H. In addition, the $\Delta^5$-hydroxy-group and *pro-R* proton at C-20 were close to each other. Only a combination of a 6α-γ-lactone system (and hence a twist-boat conformation [1] of ring B) and an α-configuration for the 7-hydroxy-group gives this stereochemistry in (19d). The chemical shifts of the *pro-R* protons at C-20 in related compounds are shown in Table 1.

Thus, both the 7-hydroxy- and the 6-methoxy-group in (19c) were shown to have the β-configuration. Ring opening of the epoxide ring of (18) therefore takes place at C-6, and is followed by attack of the nucleophile from the less hindered β-side. By analogy, the β-stereochemistry of the 6- and 7-substituents in (19a and b) was assigned. Consequently the β-configuration of the epoxide ring of (18) was established. Reduction of compound (19a) with lithium aluminium hydride followed by treatment with dilute hydrochloric acid in methanol gave compound (20), in the n.m.r. spectrum of which a triplet (*J* 8 Hz) due to 6-H was observed. This agrees with the 19,6α-lactone stereochemistry (having a

* Overall 49% from (16). In the dehydration of (15a) some starting material was recovered; recycling the recovered material increased the yield.

[17] W. K. Anderson, *J. Org. Chem.*, 1973, **38**, 2267.

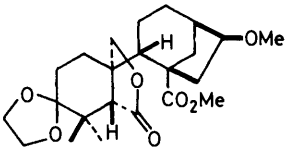
twist-boat conformation of ring B). Jones oxidation of (20) gave the ketone (21), which on reduction with sodium borohydride gave the 7α-epimer (22) as the sole product. The yields in each step from (20) to (22) were almost quantitative. Mesylation of (22) gave compound (10). As already reported,[1] ring B contraction of (10) afforded the intermediate (6) in 94% yield.

(II) *Synthesis of the Ester* (6) *from the Ester* (5).—Methylation of the 16-ol (5) with methyl iodide in the presence of sodium hydride [18] gave the methyl ether (23) quantitatively. In order to synthesise compounds (24) and (25), modification of the acyloin condensation was investigated under various conditions, with the result that (24) was obtained in *ca.* 50% yield and (25) in 25—36%. Treatment of the diol (24) with sulphuric acid in methanol gave the acetal (7), which was easily acetylated by acetic anhydride in pyridine; its 6-epimer (26) [15] resisted acetylation. The hypoiodite reaction with (26) afforded the 20-acetal (27).[15] These facts rationalised the assignments of 6β- and 6α-hydroxy-groups in structures (7) and (26), respectively. The hypoiodite reaction with compound (7) gave the lactone (12) in 75% yield.[15] Thus compound (24) was incorporated effectively into route (I).

The triol (25) was treated with toluene-*p*-sulphonic acid in methanol to give the acetal (28), whose 7-acetate (29) was subjected to the hypoiodite reaction to yield the 20-acetal (30),[15] supporting the α-configuration for the 6-hydroxy-group in (28). The 7-epimeric acetate (32) derived from (28), when subjected to the hypoiodite reaction yielded compound (32).[15] The stereochemistry of the 7-substituents in (30) and (32) was reasonably assigned from n.m.r. studies, and thus the stereochemistry of (25) was established.

The next problem was the conversion of the acetal (28) into compound (8). The 6-one (33), prepared from the acetate (29) by Jones oxidation, on reduction with lithium aluminium hydride gave (28), reduction of which with sodium borohydride regenerated (29). From these facts, the α-stereochemistry of the 6-hydroxy-groups in (28) and (29) was confirmed and the impossibility of synthesising the desired 6β-epimer by such reductions of (33) was made clear.

Subsequently, isomerisation of (33) with alkali was achieved. The 6-oxo-7β-acetate (33) on treatment with potassium hydroxide gave the 7-oxo-6β-ol (34) quantitatively. In this reaction, an equilibrium mixture of the 7-oxo-6β-ol and 6-oxo-7α-ol should be formed, with the hydroxy group in an equatorial conformation in both compounds. In the former, a non-bonded interaction between the 19-methyl and the 6β-hydroxy- group is the only unfavourable factor, whereas the latter has an unfavourable non-bonded interaction between the 19-methyl and the 6-oxo-group and also 1,3-diaxial interactions between the 7α-hydroxy-group, the 14β-proton, and the 15α-proton. This is probably the reason why the 7-oxo-6β-ol (34) was obtained as the sole product. The acyloin system is sensitive to oxidation in air under alkaline conditions to give a diketone (as diosphenol),[15]



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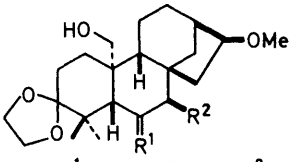
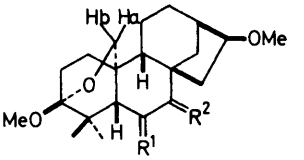
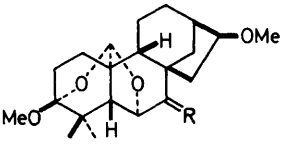


(24) $R^1$ = α—H,β—OH $R^2$ = H
(25) $R^1$ = α—OH,β—H $R^2$ = OH



(26) $R^1$ = α—OH,β—H, $R^2$ = $H_2$
(28) $R^1$ = α—OH,β—H, $R^2$ = α—H,β—OH
(29) $R^1$ = α—OH,β—H, $R^2$ = α—H,β—OAc
(31) $R^1$ = α—OH,β—H, $R^2$ = α—OAc,β—H
(33) $R^1$ = O, $R^2$ = α—H,β—OAc
(34) $R^1$ = α—H,β—OH, $R^2$ = O
(35) $R^1$ = α—H,β—OAc, $R^2$ = O
(36) $R^1$ = α—H,β—OH, $R^2$ = α—OH,β—H



(27) R = $H_2$
(30) R = α—H,β—OAc
(32) R = α—OAc,β—H

so the reaction was carried out in the absence of oxygen. Sodium borohydride or lithium aluminium hydride reduced (34) to a mixture of the epimeric 7-ols.* However Meerwein–Ponndorf reduction of the acetate (35) gave the desired 7α-ol (36) † as the sole product in 86% yield. In the transition state, attack of the reagent from the α-side seems impossible (Dreiding model), because of much bigger steric interaction between the C-14 methylene group and the methyl group of the reagent in the aluminium–ketone complex than the non-bonded interactions between the 5-, 9-, and 15-protons and the methyl groups of the reagent–ketone complex on the β-side. Acetylation gave the desired acetate (8), which was subjected to the hypoiodite reaction to give the lactone (37) and the hemiacetal acetate (38), in the ratio 2.4 : 1, in 73.5% total yield.[15]

Since our attempted conversion of (37) into (10) was not successful, compound (37) was transformed into compounds (39) and (40) as reported already.[1] Treatment with alkali then gave compound (6) and the product (20) in which ring contraction had not occurred, in the ratio 1 : 1, almost quantitatively.[1] The by-product (20) was incorporated into route (I).

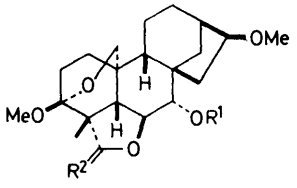
* The formation of the 7α-ol as the sole product [19] in the reduction (21) ⟶ (22) is attributable to blockage of the α-side by the C-20 methylene group because of the twist-boat form of ring B. In the case of (34), which has a chair conformation of ring B, the reaction is subject to both steric approach control and torsional strain. Consequently, a mixture of epimeric 7-ols is formed.

† Deacetylation of the 6-acetate (35) occurs at the same time, probably owing to neighbouring group participation, *i.e.* by the di-isopropoxyaluminium alkoxide group at C-7.

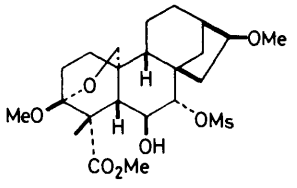
[18] *Cf.* U. E. Diner, F. Sweet, and R. K. Brown, *Canad. J. Chem.*, 1966, **44**, 1591; B. A. Stoochnoff and N. L. Benoiton, *Tetrahedron Letters*, 1973, 21.

[19] B. E. Cross, R. H. B. Galt, and J. R. Hanson, *J. Chem. Soc.* (*C*), 1963, 2944.

An attempt to convert (38) into (37) by Jones oxidation was unsuccessful. Compound (38) was therefore converted into (41) by the reactions previously reported,[1] and the latter was subjected to Jones oxidation to afford



(37) $R^1$ = Ac, $R^2$ = O
(38) $R^1$ = Ac, $R^2$ = H,OAc
(40) $R^1$ = Ms, $R^2$ = O



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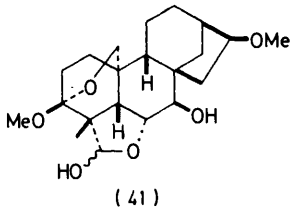
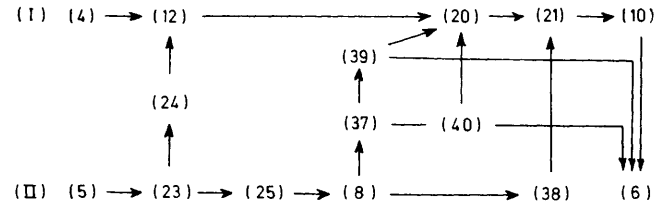


(41)

the oxo-lactone (21) in high yield. Compound (21) was incorporated into route (I).

In this way, all the compounds prepared through route (II) were effectively used for the synthesis of (6). Routes (I) and (II) are summarised in Scheme 2.

(III) *Synthesis of the Gibberellins* (2) *and* (3) *from the Ester* (6).—The major problems in the conversion of the ester (6) into the desired gibberellins are the modification of the ring A and the conversion of the methoxy- group at C-16 in ring D into an exocyclic methylene group. Since $GA_{15}$ has no oxygen function at C-3, elimination of the C-3 substituent from (6) followed by modification of C-16 was attempted. The aldehyde (6) on Jones oxidation gave a carboxylic acid (42) in 70% yield, which on treatment with ethanedithiol in the presence of boron trifluoride–ether gave the product of ethylene dithioacetalisation at C-3 accompanied by 19,20-lactonisation. Methylation with diazomethane gave the ester (43) [overall 52.5% from (42)], which on refluxing in ethanol with Raney nickel afforded a mixture of the desired product (44) and its 2,3-didehydro-derivative. Catalytic reduction of the mixture gave a single product

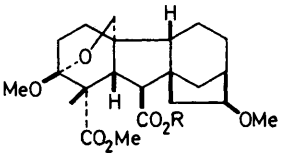



Scheme 2

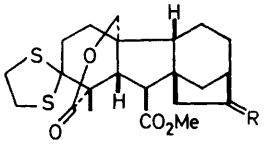
(44) [81% from (43)], which on further treatment with ethanedithiol in the presence of boron trifluoride–ether afforded the demethylation product (45) in 72% yield.

[20] P. A. Bartlett and W. S. Johnson, *Tetrahedron Letters*, 1970, 4459.

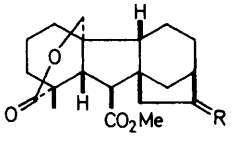
The 16-one (46), derived from (45) by Jones oxidation in 93% yield, was subjected to the Wittig reaction to give $GA_{15}$ methyl ester (47), m.p. 199—201° (lit.,[4] 198—200°), which, by the method of Johnson *et al.*[20] was treated with lithium propanethiolate in hexamethylphosphoric triamide (HMPA) to give a free carboxylic acid. The identification of the product, m.p. 263—265°, as $GA_{15}$ (2) was confirmed by spectral comparisons and by direct comparison with a sample prepared from $GA_{24}$ (48) by reduction with sodium borohydride.[21]



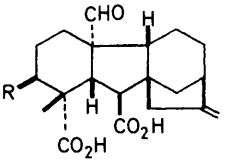
(42) R = H
(49) R = Me



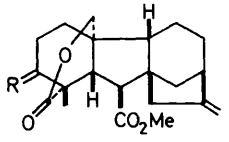
(43) R = α—H,β—OMe
(50) R = α—H,β—OH
(51) R = O
(52) R = $CH_2$



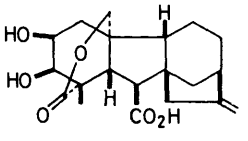
(44) R = α—H,β—OMe
(45) R = α—H,β—OH
(46) R = O
(47) R = $CH_2$



(48) R = H
(56) R = OH



(53) R = O
(54) R = α—H,β—OH
(55) R = α—OH,β—H



(57)

As $GA_{37}$ has a β-hydroxy-group at C-3, selective modifications at C-3 and C-16 of (6) were necessary. We developed a sequence capable of general application. The carboxylic acid (42) was converted into the methyl ester (49), which was treated with ethanedithiol in the presence of an increased quantity of boron trifluoride–ether for a long time. Thioacetalisation at C-3, 19,20-lactonisation, and de-*O*-methylation at C-16 occurred at the same time, and, after remethylation of the free carboxylic acid formed as a minor product with diazomethane, compound (50) was obtained as the major product [overall 60% from (42)], together with (43) [overall 22% from (42)]. The 16β-ol (50) on Jones oxidation gave the 16-one (51), which could be a common precursor of $GA_{15}$ and $GA_{37}$. Its desulphurisation with

[21] D. M. Harrison and J. MacMillan, *J. Chem. Soc.* (*C*), 1971, 631.

Raney nickel, followed by catalytic hydrogenation of the by-product (the 2,3-didehydro-derivative) gave (46), which was converted into $GA_{15}$ (2) as described above. Alternatively, the 16-one (51) was converted into the 16-methylene derivative (52) by the Wittig reaction in 93% yield, and (52) was dethioacetalised by *N*-chlorosuccinimide [22] to give the 3-one (53) in 60.5% yield. The ketone (53) on Meerwein–Ponndorf reduction with a large excess of aluminium isopropoxide [10] gave the 3β-ol (54) and its 3α-isomer (55) in 66 and 22% yields, respectively. Compound (54), m.p. 195—197°, was identical with $GA_{37}$ methyl ester [7] * (mixed m.p. and spectral data). Finally, demethylation of this methyl ester was performed as for $GA_{15}$ methyl ester, but the isolation of $GA_{37}$ from HMPA was difficult. Separation was achieved by droplet counter-current chromatography,[23] giving crystals, m.p. 228—230°, identical with authentic [7] $GA_{37}$ (3) by direct comparison and by comparison with the sample of $GA_{37}$ prepared from $GA_{36}$ (56) by reduction with sodium borohydride reduction.[8]

Thus total syntheses of $GA_{15}$ (2) and $GA_{37}$ (3) from naphthalene-1,6-diol and chemical conversions of enmein (1) into these gibberellins have been achieved. The fact that $GA_{15}$ and $GA_{37}$ were synthesised *via* common intermediates (6) and (51) is noteworthy. The synthesis of $GA_{27}$ (57) through this route should be possible, and we shall try it in the future.

Both synthetic products $GA_{15}$ and $GA_{37}$ are the optically active forms, and show biological activity as expected; this will be reported elsewhere.

## EXPERIMENTAL

M.p.s were taken with a micro hot-stage apparatus. Unless otherwise stated, i.r. spectra were recorded for KBr discs with a Hitachi EPI-S2 spectrometer and n.m.r. spectra with a Varian T-60 spectrometer for solutions in [$^2$H]chloroform with tetramethylsilane as internal standard. Mass spectra were determined with a JEOL JMS-OISG double-focusing spectrometer. Extracts were dried over anhydrous $Na_2SO_4$. Mallinckrodt silicic acid or Kieselgel (0.06—0.2 mm, Merck) was used for column chromatography, and Kieselgel G nach Stahl (Merck) for t.l.c.

ent-3β,20-*Epoxy*-3-*methoxy*-16α-(*tetrahydropyran*-2-*yloxy*)-17-*norkauran*-19,6α-*olide* (11).—A suspension of lead tetra-acetate (108 mg) and anhydrous calcium carbonate (36 mg) in dry cyclohexane was warmed for 10 min, and the alcohol (4)[2] (18 mg) and iodine (18 mg) were then added. The mixture was refluxed during irradiation by a 500 W tungsten lamp until the colour of the solution and the starting material (t.l.c.) had disappeared (1.5 h). The mixture was filtered and the filtrate and washings ($Et_2O$) of the residue were combined and washed with aqueous sodium thiosulphate and water. Drying and evaporation left a residue, which was chromatographed ($SiO_2$; $CH_2Cl_2$) to separate the lactone (11) (11 mg, 59.4%) as an amorphous compound, $\nu_{max.}$ ($CHCl_3$) 1 770 and 1 040 cm$^{-1}$, δ 1.32 (3 H, s, 4-Me), 3.40 (3 H, s, OMe), and 3.6—4.8 (7 H, m).

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6α-*olide* (12).—To a solution of compound (11) (10 mg) in methanol (1 ml) was added a catalytic amount of toluene-*p*-sulphonic acid. The mixture was warmed on a water-bath at 70 °C for 10 min. Additions of water and extraction with dichloromethane gave a residue which was chromatographed [$SiO_2$; $CH_2Cl_2$–$Me_2CO$ (19 : 1)] to separate the crystalline hydroxy-lactone (5 mg, 67%), $\nu_{max.}$ 3 480, 1 760, and 1 040 cm$^{-1}$. To a solution of this hydroxy-lactone (4 mg) in dry ether–chloroform (1 : 1; 10 ml) was added a large excess of ethereal diazomethane. To the stirred mixture, cooled in ice, boron trifluoride–etherate (one drop) was added. After 15 min, extraction with dichloromethane and treatment as usual gave a residue (5 mg), which was separated by preparative t.l.c. [$SiO_2$; $CH_2Cl_2$–$Me_2CO$ (19 : 1)] to give the methyl ether (12) (2 mg, 48%) as needles (from methanol), m.p. 220—221°, identical (i.r. spectra, mixed m.p., and t.l.c.) with an authentic sample of (12) prepared from (7).[16]

*Methyl* ent-3β,20-*Epoxy*-6α-*hydroxy*-3,16α-*dimethoxy*-17-*norkauran*-19-*oate* (13).—The lactone (12) (100 mg) in anhydrous methanol (5 ml) was refluxed for 1 h with concentrated sulphuric acid (6 drops). After cooling and neutralisation with sodium carbonate, extraction as usual gave a crystalline product (105 mg), which was recrystallised from methanol to give the *ester* (13) (85 mg) as needles, m.p. 231° (the crystal form changed at 187°), $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 720 cm$^{-1}$, δ 1.42 (3 H, s, 4-Me), 3.25 and 3.26 (each 3 H, s, 2 × OMe), 3.74 (3 H, s, $CO_2Me$), *ca.* 3.8 (1 H, m, 16-H), 3.93 and 4.73 [each 3 H, AB-type, *J* 9 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 4.33 (1 H, quint, *J* 5 Hz, 6-H) (Found: $M^+$, 394.235. $C_{22}H_{34}O_6$ requires *M*, 394.235).

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6β-*olide* (14).—To a solution of the ester (13) (36 mg) in anhydrous pyridine (3 ml) was added phosphoryl chloride (200 mg), and the mixture was stirred for 24 h at room temperature. After addition of ice–water, the mixture was extracted with dichloromethane. The usual treatment of the extract gave a crystalline product (29 mg), which was recrystallised from methanol to give the lactone (14) as needles, m.p. 217.5—218.5°, $\nu_{max.}$ 1 768 cm$^{-1}$, δ 1.33 (3 H, s, 4-Me), 3.30 and 3.44 (each 3 H, s, 2 × OMe), *ca.* 3.80 (1 H, m, 16-H), 3.90 and 4.46 [each 1 H, AB-type, *J* 9 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 4.70 (1 H, m, 6-H), $M^+$ 362.

ent-3β,20-*Epoxy*-6α-*hydroxy*-3,16α-*dimethoxy*-17-*norkauran*-19-*oic Acid* (16).—To a solution of the lactone (12) (438 mg) in acetone (30 ml) was added aqueous 30% perchloric acid (9 ml) and the mixture was refluxed for 4 h. Extraction ($CH_2Cl_2$) and treatment as usual gave a crystalline residue (485 mg), which was recrystallised from methanol to give the *hydroxy-acid* (16) (440 mg, 95%) as needles, m.p. 197—199.5°, $\nu_{max.}$ 3 400, 1 685, and 1 030 cm$^{-1}$, δ 1.50 (3 H, s, 4-Me), 3.21 and 3.33 (each 3 H, s, 2 × OMe), 3.73 (1 H, m, 16-H), and 4.04 and 4.73 [each 1 H, AB-type, *J* 9 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)] [Found: C, 63.9; H, 9.15; $M^+$, 380.215. $C_{21}H_{32}O_6$,MeOH requires C, 64.05; H, 8.8%; *M*, 380.219 ($C_{21}H_{32}O_6$)].

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-17-*norkaur*-6-*en*-19,6-*olide* (17).—To a stirred solution of the hydroxy-acid (16) (383 mg) in acetone (treated with $KMnO_4$) cooled in ice was gradually added Jones reagent (1 ml). After 20 min, the

* $GA_{37}$ methyl ester has been reported as an oil,[8] but the sample provided by Professor Takahashi was crystalline.

[22] E. J. Corey and B. W. Erickson, *J. Org. Chem.*, 1971, **36**, 3553.

[23] T. Tanimura, J. Pisano, Y. Ito, and R. Bowman, *Science*, 1970, **169**, 54.

usual work-up gave the products (341 mg), which consisted of the hydroxy lactone (15a) as the major component, $\nu_{max.}$ 3 400 and 1 755 $cm^{-1}$, δ 1.43 (3 H, s, 4-Me), 3.24 and 3.35 (each 3 H, s, 2 × OMe), 3.86 and 4.13 [each 1 H, AB-type, *J* 10 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 3.6—4.1 (1 H, m, 16-H), and the oxo-acid (15b) as minor component, $\nu_{max.}$ 1 700 $cm^{-1}$. The hydroxy-lactone (15a) (341 mg), contaminated with the oxo-acid (15b), was dissolved in anhydrous pyridine (5 ml) and cooled in ice. Thionyl chloride (0.5 ml) was then added with stirring. After stirring for 4 h at room temperature, the mixture was poured onto ice–water. Extraction with ethyl acetate, the usual treatment of the extract, and recrystallisation from methanol gave the *enol lactone* (17) [158 mg, 49% from (16)] as crystals, m.p. 272—274°, $\nu_{max.}$ 1 790 and 1 695 $cm^{-1}$, δ 1.37 (3 H, s, 4-Me), 3.26 and 3.35 (each 3 H, s, 2 × OMe), 3.74 and 4.08 [each 1 H, AB-type, *J* 8 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], 4.4—4.9 (1 H, m, 16-H), and 5.05 (1 H, d, *J* 3 Hz, 7-H) (Found: C, 70.0; H, 8.15. $C_{21}H_{28}O_5$ requires C, 69.95; H, 7.85%). From the mother liquor, a mixture (162 mg) of (17) and (15a) was obtained.

ent-3β,20;6α,7α-*Diepoxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6-*olide* (18).—To a solution of compound (17) (50 mg) in dichloromethane (20 ml) and 0.5M-sodium hydrogen carbonate (5 ml) was added *m*-chloroperbenzoic acid (100 mg) at 0 °C. After stirring for 24 h, a large amount of dichloromethane was added and the solution was washed with aqueous sodium thiosulphate and water. Drying and evaporation left a residue (62 mg), which was chromatographed ($SiO_2$) to separate the *epoxide* (18) (53 mg) as needles, m.p. 222—224° (from MeOH–$CH_2Cl_2$), $\nu_{max.}$ 1 785 $cm^{-1}$, δ 1.45 (3 H, s, 4-Me), 3.26 and 3.35 (each 3 H, s, 2 × OMe), 3.42 (1 H, s, 7-H), 3.4—3.9 (1 H, m, 16-H), and 4.20br (2 H, s, 20-$H_2$) (Found: C, 67.0; H, 7.8%; $M^+$, 376.190. $C_{21}H_{28}O_6$ requires C, 67.0; 7.5%; *M*, 376.189).

ent-3β,20-*Epoxy*-6α,7α-*dihydroxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6-*olide* (19a).—To a stirred solution of the epoxy-lactone (18) (227 mg) in dichloromethane–water (19 : 1; 15 ml) was added boron trifluoride–ether (0.05 ml) at room temperature. After 10 min, extraction ($CH_2Cl_2$) and treatment as usual gave a crystalline product (19a) (235 mg), which was recrystallised (MeOH–$CH_2Cl_2$) to give needles, m.p. 224—227°, $\nu_{max.}$ 3 400, 3 300, 1 770, 1 155, and 1 100 $cm^{-1}$, δ 1.45 (3 H, s, 4-Me), 3.26 and 3.34 (each 3 H, s, 2 × OMe), 4.06 (1 H, s, 7-OH), 3.6—4.3 (4 H), and 5.08 (1 H, s, 6-OH) (Found: C, 63.65; H, 8.05; $M^+$, 394. $C_{21}H_{30}O_7$ requires C, 63.95; H, 7.65%; *M*, 394). The amorphous *acetate* (made with $Ac_2O$–pyridine) showed δ 1.45 (3 H, s, 4-Me), 2.17 (3 H, s, OAc), 3.26 and 3.37 (each 3 H, s, 2 × OMe), *ca.* 3.75 (1 H, m, 16-H), 3.93 and 4.23 [each 1 H, AB-type, *J* 10 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 5.62 (1 H, s, 7-H) (Found: $M^+$, 436.206. $C_{23}H_{32}O_8$ requires *M*, 436.209).

ent-3β,20-*Epoxy*-6α-*fluoro*-7α-*hydroxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6-*olide* (19b).—To a stirred solution of the epoxy-lactone (18) (100 mg) in dichloromethane–water (19 : 1) (5 ml) was added aged boron trifluoride–ether (0.02 ml) at room temperature. After 10 min, extraction ($CH_2Cl_2$) and treatment as usual gave a mixture (two spots on t.l.c.) which was chromatographed [$SiO_2$; $CH_2Cl_2$–$Me_2CO$ (9 : 1)] to separate the fluoro-lactone (19b) (38 mg), needles, m.p. 230°, identical (spectroscopic data) with an authentic sample,[1] and the dihydroxy-lactone (19a) (65 mg).

ent-3β,20-*Epoxy*-7α-*hydroxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6β-*olide* (20).—To a stirred solution of the lactone (19a) (99 mg) in absolute ether (16 ml) and tetrahydrofuran (1 ml) cooled in ice was added lithium aluminium hydride (34 mg). After stirring for 3.5 h, neutralisation with dilute hydrochloric acid and extraction with ether gave a mixture (104 mg), which was dissolved in methanol (15 ml) and 10% hydrochloric acid (2 ml) and refluxed for 1 h. Extraction ($CH_2Cl_2$) and the usual work-up gave a residue (102 mg) which was chromatographed ($SiO_2$; $CH_2Cl_2$) to separate the lactone (20) (69 mg, 72.5%) as needles, m.p. 284—287° (from acetone–methanol). This compound was identical with an authentic sample (20) [1] (spectroscopic data).

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-7-*oxo*-17-*norkauran*-19,6β-*olide* (21).—To a stirred solution of the alcohol (20) (103 mg) in acetone (25 ml) at 0 °C was added Jones reagent (8 drops). After 1 h, a small amount of isopropyl alcohol was added, and the mixture was extracted ($CH_2Cl_2$). The usual treatment of the extract gave a residue (102 mg), which was chromatographed ($SiO_2$; $CH_2Cl_2$) to give the *ketone* (21) (88 mg, 85.5%) as prisms, m.p. 264—267° (decomp.) (from MeOH), $\nu_{max.}$ 1 765, 1 710, and 1 053 $cm^{-1}$, δ 1.38 (3 H, s, 4-Me), 3.24 and 3.33 (each 3 H, s, 2 × OMe), 3.54—4.0 (2 H, 20-$H_2$), and 4.87 (1 H, d, *J* 10 Hz, 6-H) (Found: C, 67.2; H, 7.45. $C_{21}H_{28}O_6$ requires C, 67.0; H, 7.5%).

ent-3β,20-*Epoxy*-7β-*hydroxy*-3,16β-*dimethoxy*-17-*norkauran*-19,6β-*olide* (22).—To a stirred solution of the ketone (21) (85 mg) in methanol (10 ml) was added sodium borohydride (90 mg) at room temperature. After 10 min, extraction ($CH_2Cl_2$) and the usual work-up gave a crystalline residue which was recrystallised from methanol to give the alcohol (22) (82 mg, 96%) as needles, m.p. 275—278°, $\nu_{max.}$ ($CHCl_3$) 3 550 and 1 770 $cm^{-1}$, δ 1.33 (3 H, s, 4-Me), 3.31 and 3.46 (each 3 H, s, 2 × OMe), 3.62 (1 H, d, *J* 4.5 Hz, 7-H), 3.90 and 4.58 [each 1 H, AB-type, *J* 10 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 4.72 (1 H, t, *J* 4 Hz, 6-H), $M^+$ 378.

ent-3β,20-*Epoxy*-7β-*mesyloxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6β-*olide* (10).—Treatment of the alcohol (22) (112 mg) with mesyl chloride (50 drops) in pyridine with stirring and cooling in ice for 42 min gave the *mesylate* (10) (129 mg, 95.5%) as needles, m.p. 265—267° (from methanol), $\nu_{max.}$ ($CHCl_3$) 1 775, 1 335, and 1 170 $cm^{-1}$, δ 1.33 (3 H, s, 4-Me), 3.16 (3 H, s, $SO_2Me$), 3.32 and 3.48 (each 3 H, s, 2 × OMe), 3.92 and 4.61 [each 1 H, AB-type, *J* 10 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], 4.45 (1 H, d, *J* 4 Hz, 7-H), and 4.88 (1 H, t, *J* 4 Hz, 6-H) (Found: C, 57.5; H, 7.15. $C_{22}H_{32}O_8S$ requires C, 57.9; H, 7.3%).

ent-3,3-*Ethylenedioxy*-20-*hydroxy*-16α-*methoxy*-17-*nor*-6,7-*secokaurane*-6,7-*dioic Acid* 6,20-*Lactone* 7-*Methyl Ester* (23).—To a solution of sodium hydride (1.35 g) (53% in mineral oil; washed with dry ether) in dimethylformamide (40 ml) was added the alcohol (5)[12] (3 g) at 0 °C under nitrogen. After stirring for 10 min, methyl iodide (2 ml) was added. After stirring for 1.5 h at room temperature, the mixture was poured into ice–water and extracted with ether. The usual work-up gave a crystalline product which was chromatographed ($SiO_2$; $CH_2Cl_2$) to give the *methyl ether* (23) (3.072 g, 99.5%) as needles, m.p. 123—125° (from $Et_2O$), $\nu_{max.}$ 1 770 and 1 725 $cm^{-1}$, δ 1.11 and 1.06 (each 3 H, s, 4-$Me_2$), 3.30 (3 H, s, OMe), 3.70 (3 H, s, $CO_2Me$), *ca.* 3.75 (1 H, m, 16-H), and 3.98 (6 H, s, O·$CH_2$·$CH_2$·O and 20-$H_2$) (Found: C, 65.45; H, 8.35. $C_{23}H_{34}O_7$ requires C, 65.4; H, 8.1%).

*Modified Acyloin Condensation with the Ester Lactone* (23); *General Procedure.*—*Method A.* To a stirred solution of sodium in liquid ammonia was added a solution of the lactone (23) in dry ether at −60 to −70 °C (bath temperature) in nitrogen. The mixture was stirred vigorously for 2 h. After addition of a small amount of methanol, ammonia was evaporated off by stirring at room temperature. After addition of water, extraction with ether and treatment as usual gave a mixture which was chromatographed ($SiO_2$; $CH_2Cl_2$–$Me_2CO$) to separate the diol (24).

*Method B.* To a stirred solution of the lactone (23) in dry ether and liquid ammonia under nitrogen was added sodium at −60 to −70 °C. The mixture was stirred vigorously for 3 h, then treated as in method A to give a residue which was chromatographed to separate the diol (24) and the triol (25) (see Table 2).

TABLE 2

Data for the modified acyloin condensation with the lactone (23)

| Na [a] | Method | (23) (g) | $Et_2O$ (ml) | liq $NH_3$ (ml) | Products and yield (%) (24) | (25) |
|---|---|---|---|---|---|---|
| 23 | A | 1.58 | 120 | 300 | 18.7 | |
| 66 | A | 1.43 | 80 | 300 | 10.6 | |
| 13 | B | 0.3 | 15 | 100 | 40.7 | |
| 25 | B | 2.0 | 15 | 300 | 50.5 | 36 |
| 32 | B | 1.5 | 25 | 300 | 49.9 | 25.4 |
| 74 | B | 0.5 | 15 | 240 | 41.5 | 32 |

[a] Atom equiv. with respect to (23).

*Products.* ent-3,3-*Ethylenedioxy*-16α-*methoxy*-17-*norkaurane*-6α,20-*diol* (24) formed prisms, m.p. 177—178° (from MeOH), $\nu_{max.}$ 3 410 $cm^{-1}$, δ ($C_5D_5N$) 1.56 and 1.63 (each 3 H, s, 4-$Me_2$), 3.27 (3 H, s, OMe), *ca.* 3.7 (1 H, m, 16-H), 3.98 (4 H, s, O·$CH_2$·$CH_2$·O), 4.36 (2 H, d, *J* 4 Hz, 20-$H_2$; changed to singlet on addition of $D_2O$), 4.26—4.74 (1 H, m, 6-H), 4.98 (1 H, s, 6-OH), and 5.73br (1 H, t, *J* 4 Hz, 20-OH) (Found: C, 69.3; H, 9.55. $C_{22}H_{36}O_5$ requires C, 69.45; H, 9.55%). ent-3,3-*Ethylenedioxy*-16α-*methoxy*-17-*norkaurane*-6β,7α,20-*triol* (25) afforded prisms, m.p. 248—250° (from MeOH), $\nu_{max.}$ 3 300—3 400, 1 110, and 1 015 $cm^{-1}$, δ ($C_5D_5N$) 1.26 and 1.81 (each 3 H, s, 4-$Me_2$), 3.32 (3 H, s, OMe), 3.91 (4 H, s, O·$CH_2$·$CH_2$·O), and 3.6—4.9 (5 H, m) (Found: C, 66.4; H, 9.15. $C_{22}H_{36}O_6$ requires C, 66.65; H, 9.15%).

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-17-*norkauran*-6α-*ol* (7).—To a solution of the diol (24) (187 mg) in chloroform (8 ml) and methanol (8 ml) cooled in ice was added concentrated sulphuric acid (1.6 ml), and the mixture was refluxed for 25 h. After cooling, it was poured onto ice–water, neutralised with sodium carbonate, and extracted with dichloromethane. The extract was treated as usual to give a crude product which was chromatographed [$SiO_2$; $CH_2Cl_2$–$Me_2CO$ (9 : 1)] to afford the *methyl acetal* (7) (142 mg, 82.5%) as needles, m.p. 158—159° (from MeOH), $\nu_{max.}$ 3 380, 1 100, 1 050, and 1 030 $cm^{-1}$, δ 1.16 and 1.25 (each 3 H, s, 4-$Me_2$), 3.28 and 3.30 (each 3 H, s, 2 × OMe), and 3.5—4.3 (2 H, m) (Found: C, 71.85; H, 9.7. $C_{21}H_{34}O_4$ requires C, 71.95; H, 9.8%). Its *acetate* (made with $Ac_2O$–pyridine) afforded crystals, m.p. 195—196°, δ 1.10 and 1.12 (each 3 H, s, 4-$Me_2$), 2.06 (3 H, s, OAc), 3.30 and 3.32 (each 3 H, s, 2 × OMe), *ca.* 3.80 (1 H, m, 16-H), 3.90 and 4.35 [each 1 H, AB-type, *J* 9 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 5.09 (1 H, sextet, *J* 10, 10, and 4 Hz, 6-H) (Found: $M^+$, 392.260. $C_{23}H_{36}O_5$ requires *M*, 392.256).

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-17-*norkaurane*-6β,7α-*diol* (28).—To a solution of the triol (25) (80 mg) in absolute methanol (20 ml) was added toluene-*p*-sulphonic acid (20 mg). The mixture was refluxed for 2 h then neutralised with sodium carbonate and evaporated *in vacuo*. The concentrate was extracted ($CH_2Cl_2$) and the extract treated as usual to give a residue which was chromatographed to yield the *methyl acetal* (28) (70 mg, 94%) as prisms, m.p. 178—180° (from MeOH), $\nu_{max.}$ 3 450 and 1 030 $cm^{-1}$, δ 1.07 and 1.22 (each 3 H, s, 4-$Me_2$), *ca.* 1.85 and *ca.* 2.15 (each 1 H, 2 × OH), 3.28 and 3.34 (each 3 H, s, 2 × OMe), 3.49 (1 H, d, *J* 4 Hz, 7-H), *ca.* 3.8 (1 H, m, 16-H), 3.84 and 4.77 [each 1 H, AB-type, *J* 9 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 4.07br (1 H, s, 6-H) (Found: C, 68.85; H, 9.45%; $M^+$, 366.240. $C_{21}H_{34}O_5$ requires C, 68.8; H, 9.5%; *M*, 366.240).

*Attempted Deacetalisation of Compounds* (7) *and* (28).—(i) Deacetalisation of (7) in aqueous 20% acetone (1.5 ml) containing 20% hydrochloric acid (0.15 ml) with stirring for 5 h did not proceed; starting material (7) was recovered quantitatively.

(ii) To a solution of (28) (10 mg) in aqueous 20% acetone (1.5 ml) was added 20% hydrochloric acid (0.15 ml), and the mixture was stirred for 1 h at room temperature. Extraction ($CH_2Cl_2$) and treatment as usual gave a residue which was chromatographed to give amorphous *ent*-3β,20-epoxy-16α-methoxy-17-norkaurane-3,6β,7α-triol (7 mg), $\nu_{max.}$ 3 450, 1 460, 1 090, and 1 020 $cm^{-1}$, δ 1.12 and 1.28 (each 3 H, s, 4-$Me_2$), 3.35 (3 H, s, OMe), 3.50 (1 H, d, *J* 4 Hz, 7-H), *ca.* 3.8 (1 H, m, 16-H), 4.12br (1 H, s, 6-H), and 3.90 and 4.82 [each 1 H, AB-type, *J* 8 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 4 Hz)].

ent-7α-*Acetoxy*-3β,20-*epoxy*-3,16α-*dimethoxy*-17-*norkauran*-6β-*ol* (29).—Compound (28) (65 mg) in acetic anhydride–pyridine (1 : 1; 2 ml) was set aside overnight at room temperature. After treatment as usual, the crude product was chromatographed ($SiO_2$; $CH_2Cl_2$) to give the *acetate* (29) (70 mg, 96.5%) as an oil, $\nu_{max.}$ 3 450, 1 720, 1 245, 1 080, and 1 030 $cm^{-1}$, δ 1.02 and 1.20 (each 3 H, s, 4-$Me_2$), 2.05 (3 H, s, OAc), 3.20 and 3.34 (each 3 H, s, 2 × OMe), *ca.* 3.78 (1 H, m, 16-H), 4.06br (1 H, s, 6-H), 4.74 (1 H, d, *J* 4 Hz, 7-H), and 3.83 and 4.84 [each 1 H, AB-type, *J* 8 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)] (Found: $M^+$, 408.251. $C_{23}H_{36}O_6$ requires *M*, 408.251).

ent-7α-*Acetoxy*-3β,20-*epoxy*-3,16α-*dimethoxy*-17-*norkauran*-6-*one* (33).—To a solution of the acetate (29) (65 mg) in acetone (2.5 ml) was added Jones reagent (5 drops) at 0 °C, and the mixture was stirred for 1 h. The usual work-up gave a crude product which was chromatographed ($SiO_2$; $CH_2Cl_2$) to give the *ketone* (33) (63 mg, 98.5%) as an oil, $\nu_{max.}$ ($CHCl_3$) 1 745, 1 725, 1 240—1 210, and 1 000 $cm^{-1}$, δ 1.18 (6 H, s, 4-$Me_2$), 2.18 (3 H, s, OAc), 3.28 and 3.30 (each 3 H, s, 2 × OMe), 3.70 (1 H, quint, *J* 5 Hz, 16-H), 4.10 and 4.43 [each 1 H, AB-type, *J* 9 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 3 Hz)], and 5.18 (1 H, s, 7-H) (Found: $M^+$, 406.232. $C_{23}H_{34}O_6$ requires *M*, 406.235).

*Reductions of the Ketone* (33).—*With lithium aluminium hydride.* To a stirred solution of (33) (57 mg) in dry ether (15 ml) cooled in ice was slowly added lithium aluminium hydride (60 mg). After refluxing for 1 h, the mixture was treated as usual and extracted with ether. The extract

gave a crude product (53 mg) which was recrystallised from methanol to afford the diol (28) (45 mg).

*With sodium borohydride.* To a stirred solution of (33) (18 mg) in methanol (4 ml) was added sodium borohydride (50 mg). After stirring for 2 h at room temperature, the usual work-up gave a crude product (16.5 mg) which was recrystallised from methanol to afford the alcohol (29) (11 mg).

ent-3β,20-*Epoxy*-6α-*hydroxy*-3,16α-*dimethoxy*-17-*norkauran*-7-*one* (34).—To a stirred solution of (33) (286 mg) in methanol (6 ml) under nitrogen was added potassium hydroxide (60 mg). After refluxing for 1 h, the mixture was immediately neutralised with dilute hydrochloric acid under a stream of nitrogen. Extraction ($CH_2Cl_2$) and the usual work-up gave a crude product which was recrystallised from methanol to afford the *acyloin* (34) (242 mg, 94.5%) as needles, m.p. 206—208°, $\nu_{max.}$ 3 450, 1 700, 1 080, and 1 028 $cm^{-1}$, δ 1.13 and 1.32 (each 3 H, s, 4-$Me_2$), 3.32 and 3.35 (each 3 H, s, 2 × OMe), 3.64 (1 H, d, *J* 4 Hz, 6-OH), *ca.* 3.8 (1 H, m, 16-H), 4.08 and 4.62 [each 1 H, AB-type, *J* 9 Hz, 20-$H_2$; each signal showed long-range coupling (*J* 1.5 and 3 Hz, respectively)], and 4.60 (1 H, dd, *J* 12 and 4 Hz, 6-H) (Found: C, 69.15; H, 8.7. $C_{21}H_{32}O_5$ requires C, 69.2; H, 8.85%).

*Reductions of the Ketone* (34).—To a solution of (34) (22 mg) in dry ether (2.5 ml) and tetrahydrofuran (2.5 ml) cooled in ice was added lithium aluminium hydride [40 mg; in dry ether (10 ml)]. After refluxing for 1 h, the usual work-up gave a mixture (23 mg) which was chromatographed ($SiO_2$; $CH_2Cl_2$–$Me_2CO$) to give a mixture of epimeric 7-ols (15 mg; homogeneous on t.l.c.). Acetylation ($Ac_2O$–pyridine) for 3 h afforded two diacetates and two 7-monoacetates, which were separated by chromatography ($SiO_2$; $CH_2Cl_2$) into a diacetate and a monoacetate fraction. N.m.r. spectra suggested that a major component of the diacetates was the 6β,7β-diacetate, whereas the major monoacetate was the 6β-hydroxy-7α-acetate.

Reduction of (34) with sodium borohydride gave the same result. In both cases, the epimeric alcohols were obtained in the ratio *ca.* 1 : 1.

ent-6α-*Acetoxy*-3β,20-*epoxy*-3,16α-*dimethoxy*-17-*norkauran*-7-*one* (35).—A mixture of (34) (106 mg) and acetic anhydride–pyridine (1 : 1; 3 ml) was set aside overnight at room temperature. The usual work-up gave the *acetate* (35) (118 mg) as needles, m.p. 245—245.5° (from MeOH), $\nu_{max.}$ 1 748, 1 715, 1 245, and 1 030 $cm^{-1}$, δ 1.10 (6 H, s, 4-$Me_2$), 2.18 (3 H, s, OAc), 3.33 (6 H, s, 2 × OMe), 3.78 (1 H, quint, *J* 5 Hz, 16-H), 4.08 and 4.63 [each 1 H, AB-type, *J* 9 Hz, 20-$H_2$, each signal showed long-range coupling (*J* 3 and 1 Hz, respectively)], and 5.53 (1 H, d, *J* 12.5 Hz, 6-H) (Found: C, 67.75; H, 8.7%; $M^+$, 406.236. $C_{23}H_{34}O_6$ requires C, 67.95; H, 8.45%; *M*, 406.236).

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-17-*norkaurane*-6α,7β-*diol* (36).—To a solution of the acetate (35) (632 mg) in isopropyl alcohol (100 ml) was added aluminium isopropoxide (1.8 g). The mixture was heated and the acetone formed was distilled off over 5 h under nitrogen. The product was obtained by extraction ($CH_2Cl_2$) as crystals (624 mg), recrystallised (MeOH–$CH_2Cl_2$) to give the *diol* (36) (492 mg, 86.3%) as prisms, m.p. 159—159.5°, $\nu_{max.}$ 3 300, 1 460, 1 100, 1 050, and 1 025 $cm^{-1}$, δ 1.17 and 1.24 (each 3 H, s, 4-$Me_2$), 3.30 and 3.33 (each 3 H, s, 2 × OMe), 3.5—4.2 (4 H), and 4.30 (1 H, one part of AB-type, *J* 9 and 3 Hz) [Found: C, 66.55; H, 9.95%: $M^+$, 366.244. $C_{21}H_{34}O_5$,-$CH_3OH$ requires C, 66.3; H, 9.6%; *M*, 366.241 ($C_{21}H_{34}O_5$)]. From the mother liquor, starting material (22 mg) was recovered.

*Jones Oxidation of the Hemiacetal* (41).—To a stirred solution of (41) [1] (14 mg) in acetone (2 ml) cooled in ice was added Jones reagent (2 drops). After 10 min, the usual work-up gave a crude product (13 mg) which was chromatographed ($SiO_2$; $CH_2Cl_2$) to afford the oxo-lactone (21) (11 mg).

ent-3,3-*Ethylenedithio*-20-*hydroxy*-16α-*methoxy*-17-*norgibberellane*-7,19-*dioic Acid* 19,20-*Lactone* 7-*Methyl Ester* (43).—To a stirred solution of the ester (6) [1] (133 mg) in acetone (25 ml) was added Jones reagent (0.3 ml) at 0 °C. After 15 min, a small amount of propan-2-ol was added. Extraction ($CH_2Cl_2$) and treatment as usual gave a crude product (117 mg) which was chromatographed ($SiO_2$; $CH_2Cl_2$–$Me_2CO$) to afford *ent*-3β,20-epoxy-3,16α-dimethoxy-17-norgibberellane-7,19-dioic acid 19-methyl ester (42) (96 mg, 70%), δ 1.45 (3 H, s, 4-Me), 3.23 and 3.26 (each 3 H, s, 2 × OMe), 3.66 (3 H, s, $CO_2Me$), and 3.6—4.3 (3 H). The acid (42) (57 mg) was dissolved in a mixture of ethanedithiol (1.5 ml) and boron trifluoride–ether (0.03 ml), and stirred for 5 days at room temperature. Extraction ($CH_2Cl_2$) and treatment as usual gave a mixture which was methylated ($CH_2N_2$) and chromatographed to yield the amorphous methyl ester (43) (32 mg, 52.5%), $\nu_{max.}$ 1 730 $cm^{-1}$, δ 1.37 (3 H, s, 4-Me), 3.23 (3 H, s, OMe), 3.28 (4 H, s, $S{\cdot}CH_2{\cdot}CH_2{\cdot}S$), 3.70 (3 H, s, $CO_2Me$), and 4.13 and 4.41 [each 1 H, AB-type, *J* 12 Hz, 20-$H_2$; lower field signal showed a long range coupling (*J* 3 Hz)].

ent-20-*Hydroxy*-16-*oxo*-17-*norgibberellane*-7,19-*dioic Acid* 19,20-*Lactone* 7-*Methyl Ester* (46).—(a) *From the ester* (43). To a solution of (43) (31 mg) in absolute ethanol (5 ml) was added W-2 Raney nickel (1.2 g) and the mixture was refluxed for 4 h. After cooling, the mixture was filtered and the filtrate evaporated *in vacuo*. The residue (24 mg) was observed to contain the 2,3-didehydro-compound in addition to (44) (n.m.r. spectrum). To a solution of the residue (24 mg) in methanol (5 ml) was added platinum oxide (catalytic amount). The mixture was stirred for 24 h in hydrogen, then filtered. The usual work-up of the filtrate gave a crude product which was chromatographed to give the ester (44) (20 mg, 81%), δ 1.13 (3 H, s, 4-Me), 3.21 (3 H, s, OMe), 3.70 (3 H, s, $CO_2Me$), and 4.06 and 4.38 [each 1 H, AB-type, *J* 12 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 2 Hz)]. To a solution of (44) (20 mg) in ethanedithiol (0.5 ml) was added boron trifluoride–ether (0.05 ml), and the mixture was stirred for 9 days at room temperature. Extraction ($CH_2Cl_2$) and treatment as usual gave a crude substance which, after treatment with diazomethane, was chromatographed ($SiO_2$; $CH_2Cl_2$) to afford the alcohol (45) (14 mg, 72%), δ 1.13 (3 H, s, 4-Me), 2.73 (1 H, one part of AB-type, *J* 12 Hz, 6-H), 3.70 (3 H, s, $CO_2Me$), 4.10 and 4.41 (each 1 H, AB-type, *J* 11 Hz, 20-$H_2$), and 4.0—4.4 (1 H, m, 16-H). To a stirred solution of (45) (13 mg) in acetone (5 ml) was gradually added Jones reagent at 0 °C until the starting material had disappeared (t.l.c.). Extraction ($CH_2Cl_2$) and treatment as usual gave the crude product (14 mg), which was chromatographed [$SiO_2$; $CH_2Cl_2$–$Me_2CO$ (9 : 1)] to separate the *ketone* (46) (12 mg, 93%), crystals (from light petroleum–$Et_2O$), m.p. 180—182°, $\nu_{max.}$ 1 730 $cm^{-1}$, δ 1.13 (3 H, s, 4-Me), 2.84 (1 H, one part of AB-type, *J* 12 Hz, 6-H), 3.72 (3 H, s, $CO_2Me$), and 4.14 and 4.44 [each 1 H, AB-type, *J* 12 Hz, 20-$H_2$; lower field signal showed long-range coupling (*J* 2 Hz)] (Found: $M^+$, 346.174. $C_{20}H_{26}O_5$ requires *M*, 346.178).

(b) *From the dithioacetal* (51). To a solution of (51) (1.5 mg) in ethanol (2 ml) was added Raney nickel (W-2), and the mixture was refluxed for 13 h. The usual work-up gave a mixture, to whose methanolic solution (3 ml) was added a catalytic amount of platinum oxide. The solution was stirred for 18 h under hydrogen, and filtered. The filtrate was evaporated *in vacuo* and the residue was chromatographed to give the *ester* (46) (1 mg, 84%), crystals, m.p. 180—182° (Found: $M^+$, 346.179. $C_{20}H_{26}O_5$ requires $M$, 346.178).

ent-20-*Hydroxygibberell*-16-*ene*-7,19-*dioic Acid* 7-*Methyl Ester* 19,20-*Lactone* (*Gibberellin* $A_{15}$ *Methyl Ester*) (47).—To a suspension of methyltriphenylphosphonium iodide (60 mg) in anhydrous tetrahydrofuran (0.5 ml) was added a solution (0.2 ml) of potassium t-butoxide [from potassium (143 mg) and t-butyl alcohol (5 ml)] under nitrogen. A solution of the ester lactone (46) (12 mg) in anhydrous tetrahydrofuran (1 ml) was added, and the mixture was stirred for 4 h at 55 °C. After addition of ice–water and neutralisation with dilute hydrochloric acid, extraction with dichloromethane and treatment as usual gave the crude product, which was chromatographed ($SiO_2$; $CH_2Cl_2$) to give *GA*$_{15}$ *methyl ester* (47) (6 mg, 50.5%) as crystals, m.p. 199—201° (from light petroleum–$Et_2O$) (lit.,[4] 198—200°), $\nu_{max.}$ ($CHCl_3$) 1 725, 1 655, and 885 $cm^{-1}$, $\delta$ 1.15 (3 H, s, 4-Me), 2.18 and 2.78 (each 1 H, AB-type, $J$ 12 Hz, 5- and 6-H), 3.70 (3 H, s, $CO_2Me$), 4.10 and 4.43 [each 1 H, AB-type, $J$ 12 Hz, 20-$H_2$; lower field signal showed long-range coupling ($J$ 2 Hz)], and 4.81 and 4.94br (each 1 H, s, 17-$H_2$) (Found: $M^+$, 344.193. $C_{21}H_{28}O_4$ requires $M$, 344.198).

ent-20-*Hydroxygibberell*-16-*ene*-7,19-*dioic Acid* 19,20-*Lactone* (*Gibberellin* $A_{15}$) (12).—To a solution of the ester (47) (4 mg) in anhydrous hexamethylphosphoric triamide (HMPA) (0.5 ml) was added a solution of lithium propane-1-thiolate (0.1 ml), generated from lithium hydride (150 mg) and propane-1-thiol (0.5 ml) in HMPA (5 ml), at room temperature under nitrogen. After stirring for 45 h, the mixture was poured onto ice–water and neutralised with 5% hydrochloric acid. Extraction ($Et_2O$) and treatment as usual gave the crude product which was chromatographed ($SiO_2$; n-$C_6H_{14}$–$CH_2Cl_2$–$Me_2CO$) to separate *GA*$_{15}$ (2) (2 mg, 52%) as crystals, m.p. 263—265° (from light petroleum–acetone) (Found: $M^+$, 330.186. $C_{20}H_{26}O_4$ requires $M$, 330.183), identical with an authentic sample (mixed m.p., n.m.r. and mass spectra, and t.l.c.) prepared from $GA_{24}$ as follows.

To a solution of gibberellin $A_{24}$ (48) (5 mg) in ethanol (1 ml) was added sodium borohydride (5 mg) at room temperature, and the mixture was stirred for 2.5 h. The usual work-up gave a crude product which was chromatographed ($SiO_2$; $CH_2Cl_2$) to afford gibberellin $A_{15}$ (2) (3 mg, 63%) as crystals, m.p. 268—270° (from light petroleum–$Et_2O$), $\delta$ 1.23 (3 H, s, 4-Me), 2.98 (1 H, one part of AB-type, $J$ 13 Hz, 6-H), 4.10 and 4.41 [each 1 H, AB-type, $J$ 12 Hz, 20-$H_2$; lower field signal showed long-range coupling ($J$ 2 Hz)], and 4.82 and 4.93br (each 1 H, s, 17-$H_2$).

ent-3,3-*Ethylenedithio*-16$\alpha$,20-*dihydroxy*-17-*norgibberellane*-7,19-*dioic Acid* 7-*Methyl Ester* 19,20-*Lactone* (50).—Treatment of the acid (42) with diazomethane yielded quantitatively the amorphous methyl ester (49), $\nu_{max.}$ ($CHCl_3$) 1 725 $cm^{-1}$, $\delta$ 1.43 (3 H, s, 4-Me), 3.21 and 3.27 (each 3 H, s, 2 × OMe), 3.61 and 3.66 (each 3 H, s, 2 × $CO_2Me$), and 3.5—4.2 (3 H, 16-H and 20-$H_2$). To a solution of (49) (130 mg) in ethanedithiol (2.5 ml) was added boron trifluoride–ether (0.1 ml), and the mixture was stirred for 8 days at room temperature. Extraction ($CH_2Cl_2$) and treatment as usual gave a crude mixture which was treated with diazomethane and then chromatographed ($SiO_2$; $CH_2Cl_2$) to separate the 16-methoxy-compound (43) (30 mg, 22%) and the 16-*ol* (50) (80 mg, 60%) crystals, m.p. 234—236° (from light petroleum–acetone), $\nu_{max.}$ ($CHCl_3$) 3 500 and 1 725 $cm^{-1}$, $\delta$ 1.37 (3 H, s, 4-Me), 1.82 (1 H, s, 16-OH), 2.66 (2 H, s), 3.30 (4 H, s, S·$CH_2$·$CH_2$·S), 3.90 (3 H, s, $CO_2Me$), 4.16 and 4.44 [each 1 H, AB-type, $J$ 12 Hz, 20-$H_2$; lower field signal showed long-range coupling ($J$ 2 Hz)], and 4.0—4.4 (1 H, 16-H) (Found: $M^+$, 438.156. $C_{22}H_{30}O_5S_2$ requires $M$, 438.153).

ent-3,3-*Ethylenedithio*-20-*hydroxy*-16-*oxo*-17-*norgibberellan*-7,19-*dioic Acid* 7-*Methyl Ester* 19,20-*Lactone* (51).—To a stirred solution of the 16-ol (50) (24 mg) in acetone (6 ml) was gradually added Jones reagent (0.05 ml) at 0 °C (care should be taken not to use an excess of the reagent). After stirring for 15 min, extraction ($CH_2Cl_2$) and treatment as usual gave the crude product, which was chromatographed ($SiO_2$; $CH_2Cl_2$) to afford the *ketone* (51) (16 mg, 67%) as crystals, m.p. >300° (from methanol), $\nu_{max.}$ ($CHCl_3$) 1 730 $cm^{-1}$, $\delta$ 1.36 (3 H, s, 4-Me), 2.66 and 2.85 (each 1 H, AB-type, $J$ 13 Hz, 5- and 6-H), 3.30 (4 H, s, S·$CH_2$·$CH_2$·S), 3.71 (3 H, s, $CO_2Me$), and 4.26 and 4.50 [each 1 H, AB-type, $J$ 12 Hz, 20-$H_2$; lower field signal showed long-range coupling ($J$ 3 Hz)] (Found: $M^+$, 436.133. $C_{22}H_{28}O_5S_2$ requires $M$, 436.137).

ent-3,3-*Ethylenedithio*-20-*hydroxygibberell*-16-*ene*-7,19-*dioic Acid* 7-*Methyl Ester* 19,20-*Lactone* (52).—To a suspension of methyltriphenylphosphonium iodide (70 mg) in anhydrous tetrahydrofuran (1 ml) was added a solution (0.2 ml) of potassium t-butoxide [from potassium (100 mg) and t-butyl alcohol (3.1 ml)] under nitrogen. A solution of the ketone (51) (33.5 mg) in anhydrous tetrahydrofuran (1 ml) was added, and the mixture was stirred for 40 min at 60 °C. After addition of ice–water and neutralisation with dilute hydrochloric acid, extraction ($CH_2Cl_2$) and treatment as usual gave a crude product which was chromatographed ($SiO_2$; $CH_2Cl_2$) to afford the amorphous olefin (52) (31 mg), $\nu_{max.}$ ($CHCl_3$) 1 725, 1 650, and 890 $cm^{-1}$, $\delta$ 1.38 (3 H, s, 4-Me), 2.55 2.81 (each 1 H, AB-type, $J$ 12 Hz, 5- and 6-H), 3.30 (4 H, s, S·$CH_2$·$CH_2$·S), 3.70 (3 H, s, $CO_2Me$), 4.16 and 4.46 [each 1 H, AB-type, $J$ 12 Hz, 20-$H_2$; lower field signal showed long-range coupling ($J$ 2 Hz)], and 4.83 and 4.93br (each 1 H, 17-$H_2$).

ent-20-*Hydroxy*-3-*oxogibberell*-16-*ene*-7,19-*dioic Acid* 7-*Methyl Ester* 19,20-*Lactone* (53).—To a solution of the dithioacetal (52) (11 mg) in aqueous 80% acetone (1.5 ml) were added *N*-chlorosuccinimide (15 mg) and silver nitrate (21.3 mg) at room temperature. The mixture was stirred for 2.5 h and treated at 1 min intervals with saturated aqueous sodium sulphite, saturated aqueous sodium carbonate, and brine (1 drop each). Extraction ($CH_2Cl_2$) and the usual treatment gave a crude product (11 mg), which was chromatographed ($SiO_2$; $CH_2Cl_2$) to separate the ketone (53) (5.5 mg, 60.5%) as needles, m.p. 248—250° (from light petroleum–acetone) (lit.,[24] 248—250°), $\nu_{max.}$ ($CHCl_3$) 1 735, 1 710, 1 650, and 886 $cm^{-1}$, $\delta$ 1.24 (3 H, s, 4-Me), 2.96 (1 H, one part of AB-type, $J$ 12 Hz, 6-H), 3.71 (3 H, s, $CO_2Me$), 4.43 and 4.69 [each 1 H, AB-type, $J$ 12 Hz, 20-$H_2$; lower field signal showed long-range coupling ($J$ 2 Hz)], and 4.83 and 4.95br (each 1 H, s, 17-$H_2$) (Found: $M^+$, 358.177. Calc. for $C_{21}H_{26}O_5$: $M$, 358.178).

[24] B. E. Cross and J. C. Stewart, *J. Chem. Soc.* (*C*), 1971, 245.

ent-3α,20-*Dihydroxygibberell*-16-*ene*-7,19-*dioic Acid* 7-*Methyl Ester* 19,20-*Lactone* (*Gibberellin* $A_{37}$ *Methyl Ester*) (54).—The ketone (53) (10.5 mg) in propan-2-ol (20 ml) was heated with aluminium isopropoxide (1 g). Propan-2-ol and the acetone formed were distilled from the mixture, and at the same time propan-2-ol was gradually added. After 1.5 h, the mixture was condensed and extracted ($CH_2Cl_2$). The extract was treated as usual to give a crude substance (12.5 mg) which was chromatographed ($SiO_2$; $CH_2Cl_2$–$Me_2CO$) to separate two products: (i) *gibberellin* $A_{37}$ *methyl ester* (54) (7 mg, 66%), obtained as crystals (from light petroleum–$Et_2O$), m.p. 195—197°, $\nu_{max.}$ ($CCl_4$) 3 570, 2 430, 1 735, 1 655, and 882 $cm^{-1}$, δ 1.20 (3 H, s, 4-Me), 2.78 (2 H, s, 5- and 6-H), 3.70 (3 H, s, $CO_2Me$), 4.12 and 4.47 [each 1 H, AB-type, $J$ 12 Hz; lower field signal showed long-range coupling ($J$ 2 Hz)], and 4.84 and 4.93br (each 1 H, s, 17-$H_2$) (Found: $M^+$, 360.189. $C_{21}H_{28}O_5$ requires $M$, 360.193), identical with an authentic sample (mixed m.p., mass, n.m.r., and i.r. spectra, and t.l.c.); and (ii) material (2.3 mg, 22%) which contained the 3-epimer (55) of $GA_{37}$ methyl ester as the main component, and which was not investigated in detail.

ent-3α,20-*Dihydroxygibberell*-16-*ene*-7,19-*dioic Acid* 19,20-*Lactone* (*Gibberellin* $A_{37}$) (3).—The methyl ester (54) (7.5 mg) was dissolved in a solution (0.5 ml) of lithium propane-1-thiolate in HMPA [from lithium hydride (0.3 g) and propane-1-thiol (1 ml) in HMPA (10 ml)], and the mixture was stirred at room temperature under nitrogen. After 3 h, the mixture was poured onto ice–water and neutralised with 5% hydrochloric acid. Extraction with ethyl acetate and treatment as usual to give a crude mixture which was chromatographed ($SiO_2$; $CH_2Cl_2$). Separation of HMPA from $GA_{37}$ was difficult, and the mixture was therefore subjected to droplet counter-current chromatography [$CHCl_3$–MeOH–$H_2O$ (5 : 5 : 3)]. Evaporation of the solvents from the fractions containing $GA_{37}$ left a residue, which was chromatographed [$SiO_2$; ethyl acetate–petroleum–acetic acid (6 : 4 : 1)] to afford gibberellin $A_{37}$ (3) (1.5 mg, 21%) as needles (from ethyl acetate–petroleum), m.p. 228—230°, $\nu_{max.}$ 3 550, 1 710, 1 685, 1 655, and 878 $cm^{-1}$; *m/e* 346 ($M^+$, 48%), 328 (25), 318 (34), 310 (12), 300 (30), 282 (56), 278 (17), 270 (45), 256 (22), 237 (28), and 222 (base peak), identical (i.r., n.m.r., and mass spectra, m.p. and mixed m.p., and t.l.c.) with an authentic sample derived from gibberellin $A_{36}$.

We thank Professor N. Takahashi, University of Tokyo, and Dr. J. MacMillan, University of Bristol, for authentic samples of $GA_{37}$ and its methyl ester and $GA_{36}$ and copies of their n.m.r. and mass spectra, and for $GA_{24}$ and $GA_{37}$, respectively. We also thank Professor T. Okamoto, University of Tokyo, for a sample of $GA_{15}$, and Dr. B. E. Cross, University of Leeds, for a sample of $GA_{15}$ 17-norketone and copies of the i.r. spectra of this compound and $GA_{15}$. Thanks are also due to Professor C. Tani and Dr. N. Nagakura, Kobe Women's College of Pharmacy, for help with the droplet counter-current chromatography, and to Dr. H. Yoshioka and Dr. A. Mine, Sumitomo Chem. Ind. Co. Ltd., for the bioassay. This work was supported in part by a Grant-in-Aid from the Ministry of Education.

[6/1459 *Received*, 26*th July*, 1976]