Terpenoids. Part XXXVIII.[1] Ring B Contraction of Kauranolides and Related Compounds into Gibberellane-type Compounds

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A detailed investigation of ring B contraction has been carried out with several derivatives containing the *ent*-3β,20-epoxy-3,16α-dimethoxy-17-norkaurane skeleton (1). The 19,6β-lactone 7α-methanesulphonate (3) on treatment with base and subsequent methylation gave the gibberellane aldehyde (8) and the epimeric norkaurane derivative (9). The 6β-hydroxy-7α-methanesulphonate (4) on similar treatment gave a similar result. The 19,6α-lactone 7α-methanesulphonate (6) on treatment with potassium hydroxide in t-butyl alcohol–water and subsequent methylation afforded only the desired product (8), in almost quantitative yield. The ring B contraction reaction did not proceed with the 6β-methanesulphonate 7α-acetate (7). The results are rationalised in terms of stereochemical considerations.

IN the course of the synthesis of the methyl esters of gibberellins A_{15} and A_{37},[2] a study of the ring contraction of kauranes to gibberellanes was required. The details of this investigation are reported here. All the kaurane derivatives studied [(2)—(7)] had the *ent*-3β,20-epoxy-3,16α-dimethoxy-17-norkaurane skeleton (1), with ring A fixed in a boat conformation, and oxygenated at positions 6, 7, and 19; stereoisomers at positions 6 and 7 were included. Compounds (2)—(6) have a methylsulphonyloxy-group as the leaving group at C-7; compound (7) has the same leaving group at C-6. The desired product was the gibberellane (8). The rearrangement of kauranes with ring A in a chair conformation into gibberellane 7-aldehyde derivatives was first carried out by Galt and Hanson,[3] and many applications[4] have been published since.

The methanesulphonate (2) was derived from the 7β-ol (9).[2,†] The 6β,7α-epimer (3) was obtained by hydrolysis of the 7α-acetate (10)[1] to the 7α-ol (11) followed by methylsulphonylation. The methanesulphonate (4) was synthesised from the 7α-ol (12) derived from (10) by alkaline hydrolysis and subsequent methylation. The corresponding 19-aldehyde (5) was derived from the hemiacetal acetate (13)[1] by alkaline hydrolysis to the 6β,7α-dihydroxy-19-aldehyde (14) followed by 7-methylsulphonylation. The 19,6α-lactone 7α-methanesulphonate (6)[2,†] is known. Compound (7) was obtained from (12) by acetylation [to (15)] followed by methylsulphonylation.

Attempts to convert these materials into gibberellanes *via* ring B contraction were carried out by two methods: (I) refluxing with sodium methoxide in methanol followed by methylation of the product with diazomethane and (II) refluxing with potassium hydroxide in t-butyl alcohol–water (40 : 1) followed by methylation of the product, as described in the Experimental section. Treatment of compound (2) by method II resulted in intractable material. The compound (3), by method I or II gave the desired gibberellane derivative (8)[2,†] and the epimeric hydroxy-lactone (9)[2,†] in the ratio *ca.* 1 : 1 in each case. Compound (4) by method II also gave compounds (8) and (9) in the ratio 1 : 1. When compound (4) was treated by method I for a long time, compounds (8) and (9) were obtained in 14 and 48% yields, respectively. The low yield of the desired compound (8) in this case is probably due to decomposition of the unstable aldehyde product. Compound (5) by method II afforded only the hemiacetal (16), in 60% yield. The structure of (16) was confirmed by the

† Details will be published in the full paper on the synthesis of C_{20} gibberellins.

[1] Part XXXVII, M. Node, H. Hori, and E. Fujita, *Chem. and Pharm. Bull.* (*Japan*), in the press.

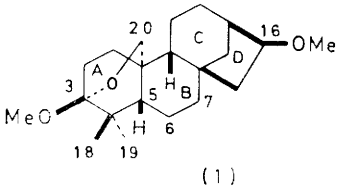
[2] M. Node, H. Hori, and E. Fujita, *J.C.S. Chem. Comm.*, 1975, 898.

[3] R. H. B. Galt and J. R. Hanson, *J. Chem. Soc.*, 1965, 1565.

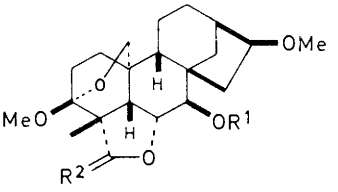
[4] (*a*) B. E. Cross, K. Norton, and J. C. Stewart, *J. Chem. Soc.* (*C*), 1968, 1045; (*b*) P. Hedden and J. MacMillan, *Tetrahedron Letters*, 1971, 4939; (*c*) J. R. Hanson and J. Hawker, *ibid.*, 1972, 4299; (*d*) J. R. Bearder and J. MacMillan, *Phytochemistry*, 1973, **12**, 2173; (*e*) P. Hedden, J. MacMillan, and B. P. Phinney, *J.C.S. Perkin I*, 1974, 587.

formation of the acetate of (9) by acetylation followed by Jones oxidation. An almost quantitative yield of the desired product (8) was obtained, when compound (6) was treated by method II. The reaction with compound (7) will be separately described later.

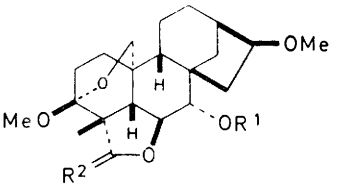
A general prerequisite for smooth ring B contraction is an antiperiplanar stereochemistry between the migrating bond and the leaving group. Of the materials (2)—(6) the norkaurane 19,6α-lactone derivatives, *i.e.* (2) and (6), are expected to have a twist boat conformation of ring B, since the twist boat form of ring B in compound (17) has been established by an *X*-ray analysis[5] and supported by n.m.r. investigations[6] of several 7-hydroxykaurenolide derivatives. Indeed Dreiding models of (2) and (6) show the preference for a boat-like conformation rather than a chair conformation of ring B because of large non-bonded interactions in the latter.* by hydrolysis, followed by a change in the conformation of ring B from a twist boat to the more favoured chair conformation. In the compound (6), ring A is fixed in a boat conformation as described above; hence the 19-substituent is fixed in a quasiequatorial conformation, which is not changed in the lactone-cleaved compound. When ring B in the lactone-cleaved product assumes a chair form, the non-bonded interaction between the 19-substituent and 6α-axial oxygen function is decreased to a minimum when this conformation is stabilised. Thus, the required antiperiplanar stereochemistry is achieved, and is maintained in the transition state, so that smooth rearrangement can take place. In compound (4), the migrating C(5)–C(6) bond and the leaving C(7)–O bond are originally in an antiperiplanar conformation; thus the ring B contraction product (8) is formed. On the other hand, ring B is subject to change to a boat-



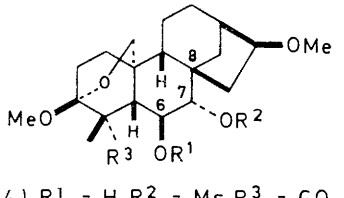
(1)



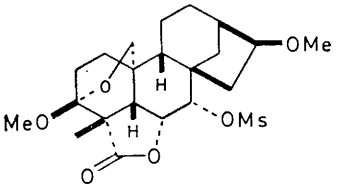
(2) R^1 = Ms, R^2 = O
(9) R^1 = H, R^2 = O
(16) R^1 = H, R^2 = H,OH



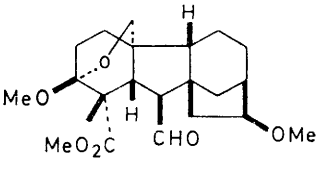
(3) R^1 = Ms, R^2 = O
(10) R^1 = Ac, R^2 = O
(11) R^1 = H, R^2 = O
(13) R^1 = Ac, R^2 = H,OAc



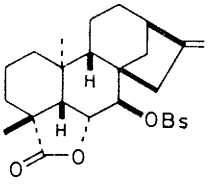
(4) R^1 = H, R^2 = Ms, R^3 = CO_2Me
(5) R^1 = H, R^2 = Ms, R^3 = CHO
(7) R^1 = Ms, R^2 = Ac, R^3 = CO_2Me
(12) R^1 = R^2 = H, R^3 = CO_2Me
(14) R^1 = R^2 = H, R^3 = CHO
(15) R^1 = H, R^2 = Ac, R^3 = CO_2Me



(6)



(8)



(17)

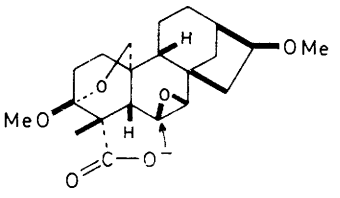
In compounds (3)—(5), however, the chair-like conformation is preferred for ring B.† On the basis of the foregoing considerations, an antiperiplanar stereochemistry of the C(5)–C(6) and C(7)–O bonds is expected in compounds (2)—(5). In compound (6), such an antiperiplanar stereochemistry seems not to be favoured. Nevertheless, this compound gave the best result in the ring contraction experiment. This fact may be explained in terms of initial opening of the γ-lactone ring like conformation in order to release the non-bonded interaction between the 6β- and 19-substituents; hence the formation of the 6,7β-epoxide (18) and subsequent ring-opening by attack of the 19-carboxylate from the α-side result in the epimeric hydroxy-lactone (9). That

* Ring C may have a boat conformation.[5] If so, a large non-bonded interaction between the 11α- and 20-hydrogen atoms would be expected. If ring C has a chair conformation, then large non-bonded interactions between H-12α and -20 and between H-14α and -20 should occur.

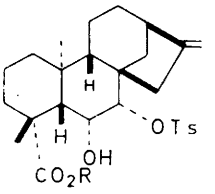
† Compound (3) cannot have a boat conformation of ring B. Although reasonable assignments for H-6 and -7 in the n.m.r. spectra of compounds (4) and (5) are difficult because of overlap with other CH·O signals, the coupling patterns of H-6 and -7 in compounds (7) and (15) support the chair conformation of ring B in these cases (see Experimental section). By analogy, compounds (4) and (5) are most likely to have a chair conformation of ring B.

[5] J. R. Hanson, G. M. McLaughlin, and G. A. Sim, *J.C.S. Perkin II*, 1972, 1124.
[6] J. R. Hanson, *Tetrahedron*, 1966, **22**, 1701.

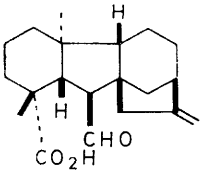
the same result was obtained in the case of (3) indicates a minimal likelihood of simultaneous γ-lactone ring



(18)



(19) R = H
(20) R = Me

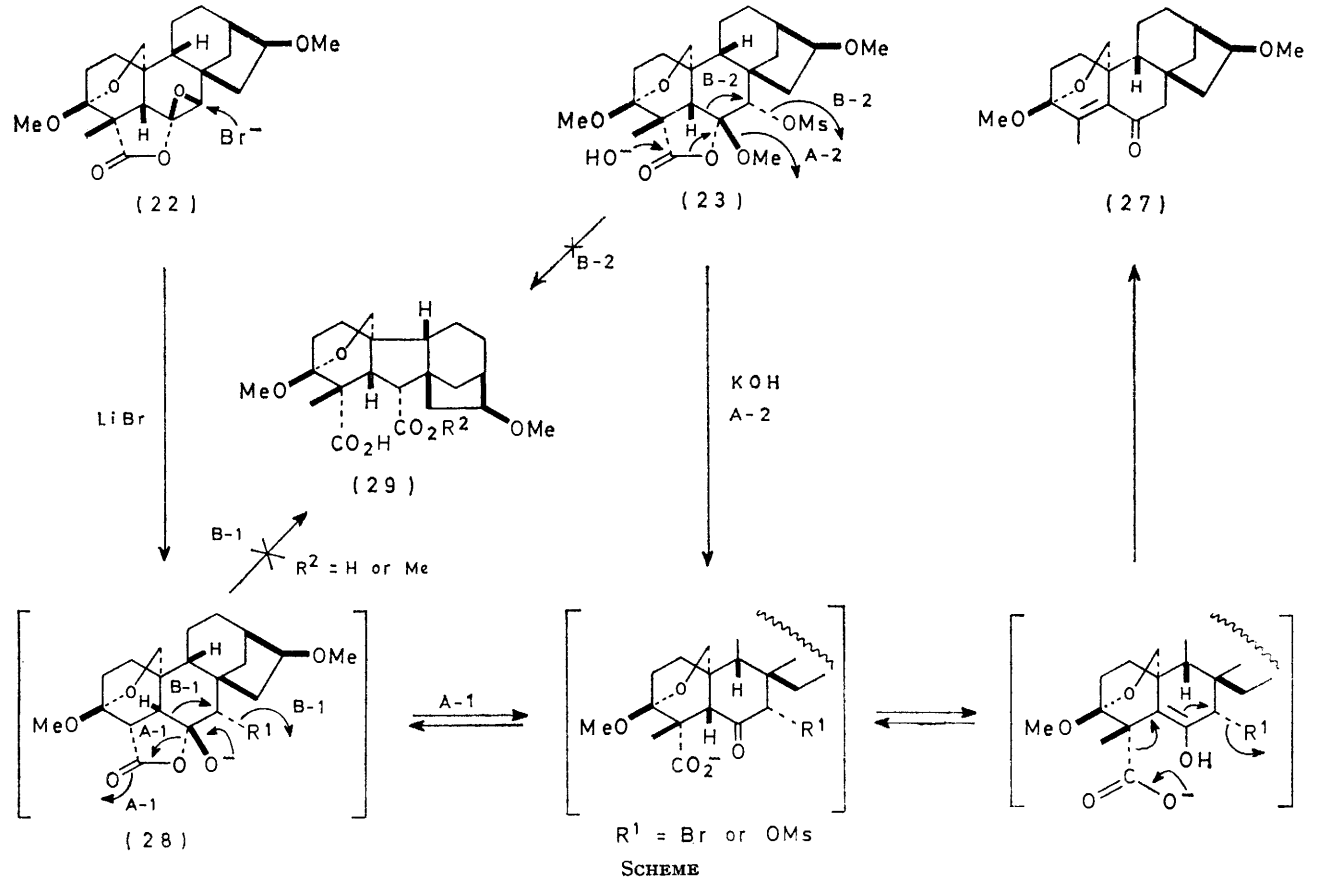


(21)

opening and the ring B contraction; presumably ring opening of the γ-lactone is followed by the same process as in the case of (4). In the case of (5) also, ring B contraction must occur in part, but the failure to isolate the corresponding gibberellane dialdehyde is probably due to decomposition of the unstable product. In the reaction with compound (2), which gave only a mixture of many products, no detailed investigation was carried out. The fact that compound (2), apparently the most suitable compound for ring B contraction, did not give a good result is probably attributable to initial lactone ring opening followed by a change from a boat-like to a chair-like conformation of ring B, making it impossible to keep the original favourable conformation.

The product (8) is the thermodynamically more stable secondary product formed by epimerisation of the initial 6α-aldehyde product under basic conditions.[7]

Bearder and MacMillan [4d] explained the reactions of the hydroxy-acid (19) with sodium hydride or collidine giving 41% of gibberellane product (21) in terms of intramolecular abstraction of the proton of the 6α-hydroxy-group by the 19-carboxylate, because the same reactions with the methyl ester (20) did not give any ring B contraction product. In compound (20) acetylation of the 6α-hydroxy-group does not occur because of steric interaction with the 19-substituent, whereas methylsulphonylation of the 6β-hydroxy-group of compound (15) gives the methanesulphonate (7). Thus the steric compression at the 6β-hydroxy-group in (4) or (15) is smaller than that at the 6α-hydroxy-group in (20). Therefore, intramolecular abstraction of the proton at the 6β-hydroxy-group in the foregoing reactions with (4) seems not as effective as in the reaction with (19), but a small contribution is not ruled out.

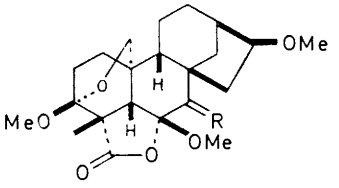


(22) (23) (27) (29) (28)

SCHEME

[7] *Cf.* M. Somei and T. Okamoto, *Yakugaku Zasshi*, 1972, **92**, 397.

Previously, we attempted to bring about the rearrangement reaction with compounds (22) [2],† and (23). The latter compound was derived from (22) *via* (24), (25), and (26), by successive reaction with boron trifluoride–ether in methanol–dichloromethane, oxidation, reduction with sodium borohydride, and methylsulphonylation. Treatment of (22) with lithium bromide in hexamethylphosphoric triamide [8] gave a conjugated ketone (27) as the major product. Treatment of (23) with potassium hydroxide in aqueous t-butyl alcohol gave the same product. The reactions are suggested to proceed by pathways A-1 and A-2 in the Scheme.



(24) R = α-H, β-OH
(25) R = O
(26) R = α-OH, β-H

In order to obtain gibberellanes (29) in these reactions, the concerted pathways B-1 and B-2 in the Scheme are required. However ring B is present in a twist boat conformation in (28) (in which R′ is Br) and (23); hence the C(5)–C(6) and C(7)–Br bonds in (28) and the C(5)–C(6) and C(7)–O bonds in (23) cannot have antiperiplanar stereochemistry. Thus, these reactions can not proceed through pathways B-1 and B-2, but take place through A-1 and A-2 to yield compound (27).

Finally, the foregoing methods I and II were applied to compound (7), which offered a model for the biosynthetic ring contraction with extrusion of C-7 in contrast to the observed ring contractions with extrusion of C-7. The desired product (8) was obtained only in low yield, the starting material being largely unchanged. The low yield may be due to the difficulty of maintaining an antiperiplanar conformation of the C(8)–C(7) and C(6)–O bonds in the transition state, because of distortion of the chair ring B conformation by non-bonded interaction between the 19- and 6-substituents.

In conclusion, we have established that treatment of compound (6) by method II provides the best synthesis of the gibberellane (8).

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 (tetramethylsilane as internal standard). Mass spectra were determined with a JEOL JMS-OISG double-focusing spectrometer, and u.v. spectra with a Hitachi EPS-3 spectrometer for solutions in methanol. Extracts were dried over sodium sulphate. Mallinckrodt silicic acid or Kieselgel (0.06—0.2 mm; Merck) was used for column chromatography, and Kieselgel G (Merck) for t.l.c.

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-7α-*methylsulphonyloxy*-17-*norkauran*-19,6β-*olide* (2).—The alcohol (9) [2] (19 mg) and methanesulphonyl chloride (20 drops) in pyridine (1.5 ml) were stirred at room temperature for 2 h; the usual work-up gave the amorphous methanesulphonate (2) (14 mg), δ 1.38 (3 H, s, 4-Me), 3.20 (3 H, s, OMs), 3.25 and 3.38 (each 3 H, s, 2 × OMe), 3.6—4.2 (16H and 20-H_2), 4.65 (1 H, t, *J* 8 Hz, 6-H), and 5.13 (1 H, d, *J* 8 Hz, 7-H); *m/e* 456 (M^+, 100%), 424 (14), 360 (46.5), and 328 (42).

ent-3β,20-*Epoxy*-3,16α-*dimethoxy*-7β-*methylsulphonyloxy*-17-*norkauran*-19,6α-*olide* (3).—To a stirred solution of the acetate (10) [1] (60 mg) in methanol (3 ml) and water (0.5 ml) was added sodium carbonate (40 mg) at room temperature. After 1 h, acidification with dilute hydrochloric acid and extraction with dichloromethane gave a mixture which was chromatographed [SiO_2; CH_2Cl_2–Me_2CO (4 : 1)] to separate the *alcohol* (11) (42 mg) as needles, m.p. 242—244° (from MeOH), δ 1.36 (3 H, s, 4-Me), 3.24 and 3.40 (each 3 H, s, 2 × OMe), *ca.* 3.8 (16-H), 3.82 (1 H, d, *J* 11 Hz, 7-H), 4.40 (1 H, t, *J* 11 Hz, 6-H), and 3.93 and 4.68 [each 1 H, AB type, *J* 11 Hz, 20-H_2; lower field signal showed long range coupling (*J* 3 Hz)] (Found: C, 66.6; H, 8.3. $C_{21}H_{30}O_6$ requires C, 66.65; H, 8.0%), and a carboxylic acid (12 mg) which was methylated (CH_2N_2) to give *methyl* ent-3β,20-*epoxy*-6α,7β-*dihydroxy*-3,16α-*dimethoxy*-17-*norkauran*-19-*oate* (12) (12 mg) as needles, m.p. 240—242.5° (from MeOH), $\nu_{max.}$ 3 450, 1 700, and 1 252 cm^{-1}, δ 1.42 (3 H, s, 4-Me), 3.26 and 3.33 (each 3 H, s, 2 × OMe), 3.73 (3 H, s, CO_2Me), and 3.4—4.8 (6-, 7-, and 16-H, and 20-H_2) (Found: M^+, 410.235. $C_{22}H_{34}O_7$ requires *M*, 410.230). Treatment of the alcohol (11) (9 mg) with methanesulphonyl chloride (10 drops) in pyridine (0.5 ml) with stirring at room temperature for 6 h gave the *methanesulphonate* (3) (11 mg) as prisms, m.p. 214—216° (from MeOH), $\nu_{max.}$ 1 785, 1 350, and 1 173 cm^{-1}, δ 1.33 (3 H, s, 4-Me), 3.20 (3 H, s, OMs), 3.33 and 3.37 (each 3 H, s, 2 × OMe), *ca.* 3.9 (1 H, m, 16-H), 3.90 and *ca.* 4.80 [each 1 H, AB type, *J* 10 Hz, 20-H_2; lower field signal showed long range coupling (*J* 3 Hz)], 4.42 (1 H, t, *J* 10 Hz, 6-H), and 4.76 (1 H, d, *J* 10 Hz, 7-H) (Found: M^+, 456.184. $C_{22}H_{32}O_8$ requires *M*, 456.181).

Methyl ent-3β,20-*Epoxy*-6α-*hydroxy*-3,16α-*dimethoxy*-7β-*methylsulphonyloxy*-17-*norkauran*-19-*oate* (4).—Treatment of the diol (12) (20 mg) with methanesulphonyl chloride (6 drops) in pyridine with stirring at room temperature for 2.5 h gave the *methanesulphonate* (4) (17 mg) as needles, m.p. 203—205° (from MeOH), $\nu_{max.}$ 3 550, 1 715, 1 335, 1 120, and 917 cm^{-1}, δ 1.45 (3 H, s, 4-Me), 3.15 (3 H, s, OMs), 3.28, 3.35 (each 3 H, s, 2 × OMe), 3.73 (3 H, s, CO_2Me), and 3.5—4.8 (6-, 7-, and 16-H, and 20-H_2) (Found: M^+, 488.208. $C_{23}H_{36}O_9S$ requires *M*, 488.208).

ent-3β,20-*Epoxy*-6α-*hydroxy*-3,16α-*dimethoxy*-7β-*methylsulphonyloxy*-17-*norkauran*-19-*al* (5).—To a solution of the crude hemiacetal acetate (13) [1] (65 mg) contaminated by the lactone (10) in methanol (10 ml) was added potassium hydroxide (100 mg) in water (0.5 ml). After refluxing for 50 min, addition of water, acidification with dilute hydrochloric acid, and extraction with dichloromethane gave a mixture, which was chromatographed [SiO_2: CH_2Cl_2–Me_2CO (17 : 3)] to separate the *dihydroxy-aldehyde* (14) (27 mg) as needles, m.p. 151—155° (decomp.) (from MeOH), $\nu_{max.}$ 3 450, 3 280, 1 710, and 1 010 cm^{-1}, δ 1.30 (3 H, s, 4-Me), 3.30 and 3.33 (each 3 H, s, 2 × OMe),

† See footnote p. 2144.

[8] B. Rickborn and R. M. Gerkin, *J. Amer. Chem. Soc.*, 1971, **93**, 1693.

3.5—4.5 (6-, 7-, and 16-H, and 20-H_2), and 10.22 (1 H, s, CHO) (Found: M^+, 380.217. $C_{21}H_{32}O_6$ requires M, 380.219), and a carboxylic acid (10 mg) which was treated with diazomethane to give the methyl ester (12) (11 mg). Treatment of the diol (14) (58 mg) with methanesulphonyl chloride (7 drops) in pyridine (1.5 ml) with stirring at room temperature for 2 h gave the *7α-methanesulphonate* (5) (38 mg) as needles, m.p. 146—149° (from MeOH), $\nu_{max.}$ 3 400, 1 715, 1 335, and 1 170 cm^{-1}, δ 1.34 (3 H, s, 4-Me), 1.60 (1 H, s, OH), 3.17 (3 H, s, OMs), 3.30 and 3.32 (each 3 H, s, 2 × OMe), 3.5—4.6 (6-, 7-, and 16-H, and 20-H_2), and 10.17 (1 H, s, CHO) (Found: C, 55.55; H, 7.85%; M^+, 458.198. $C_{22}H_{34}O_8S,H_2O$ requires C, 55.45; H, 7.6%. $C_{22}H_{34}O_8S$ requires M, 458.197).

Methyl ent-7β-*Acetoxy*-3β,20-*epoxy*-3,16α-*dimethoxy*-6α-*methylsulphonyloxy*-17-*norkauran*-19-*oate* (7).—A solution of the diol (12) (10 mg) in acetic anhydride–pyridine (1 : 1; 1.5 ml) was kept for 12 h at room temperature. The mixture was treated as usual to give the *acetate* (15) (9 mg) as crystals, m.p. 215—217.5° (from MeOH), δ 1.43 (3 H, s, 4-Me), 2.13 (3 H, s, OAc), 3.28 and 3.33 (each 3 H, s, 2 × OMe), 3.73 (3 H, s, CO_2Me), *ca.* 3.80 (1 H, m, 16-H), 3.96 and *ca.* 4.75 [each 1 H, AB type, J 9.5 Hz, 20-H_2; lower field signal showed long-range coupling (J 3 Hz)], 4.30 (1 H, t, J 10 Hz, 6-H), and 4.67 (1 H, d, J 10 Hz, 7-H) (Found: M^+, 452.242. $C_{24}H_{36}O_8$ requires M, 452.241). Treatment of (15) (14 mg) with methanesulphonyl chloride (15 drops) in pyridine (1.5 ml) for 3 days at room temperature gave the *methanesulphonate* (7) (13 mg) as needles, m.p. 193—194° (from MeOH), $\nu_{max.}$ 1 740, 1 715, 1 350, 1 225, and 1 180 cm^{-1}, δ 1.41 (3 H, s, 4-Me), 2.16 (3 H, s, OAc), 3.01 (3 H, s, OMs), 3.27 and 3.31 (each 3 H, s, 2 × OMe), 3.83 (3 H, s, CO_2Me), 3.6—4.1 (16-H and one proton of 20-H_2), *ca.* 4.78 (1 H, one part of AB type, J 10 Hz, 20-H), 4.90 (1 H, d, J 10 Hz, 7-H), and 5.49 (1 H, t, J 10 Hz, 6-H) (Found: C, 56.35; H, 7.65. $C_{25}H_{38}O_{10}S$ requires C, 56.6; H, 7.2%).

Ring Contraction: General Procedure.—Method I. To a solution of sodium methoxide (*ca.* 30 mol. equiv.) in methanol was added the methanesulphonate, and the mixture was refluxed for several hours in a stream of nitrogen. The usual treatment [addition of water, acidification (dil. HCl), and extraction (CH_2Cl_2)] gave a crude product, which was treated with diazomethane in ether–methanol. The solution was evaporated *in vacuo*, and the residue was chromatographed (SiO_2; CH_2Cl_2–Me_2CO).

Method II. The methanesulphonate was refluxed with a solution of potassium hydroxide (*ca.* 50 mol. equiv.) in t-butyl alcohol–water (40 : 1) and the mixture was treated as in method I.

Results of ring contractions

Material; wt (mg)	Reagent	Reaction time (h)	Products; yield (%)
(2); 9	KOH	5	Intractable products
(3); 65	KOH	1	(8); 49.6 and (9); 42.5
(3); 10	NaOMe	1	(8); 47 and (9); 48
(4); 122	KOH	2	(8); 39 and (9); 44
(4); 19	NaOMe	9	(8); 14 and (9); 48
(5); 21	KOH	1.5	(16); 60
(6); 98	KOH	2	(8); 94
(7); 16	KOH	2	(8); <17
12	NaOMe	7	(8); *ca.* 19

The results are shown in the Table. *Methyl* ent-3β,20-*epoxy*-3,16α-*dimethoxy*-7-*oxo*-17-*norgibberellan*-19-*oate* (8) [2] had m.p. 123—124° (from MeOH), δ 1.48 (3 H, s, 4-Me), 3.22 and 3.27 (each 3 H, s, 2 × OMe), 3.60 (3 H, s, CO_2Me), 3.5—4.2 (16-H and 20-H_2), and 9.75 (1 H, d, J 2 Hz, 7-H) (Found: M^+, 392.226. $C_{22}H_{32}O_6$ requires M, 392.220). *ent*-3β,20-Epoxy-7α-hydroxy-3,16α-dimethoxy-17-norkauran-19,6β-olide (9) (prisms) had m.p. 284—287° (from Me_2CO–MeOH), $\nu_{max.}$ 3 400, 1 765, and 1 050 cm^{-1}, δ 1.35 (3 H, s, 4-Me), 2.9br (1 H, s, OH), 3.27 and 3.38 (each 3 H, s, 2 × OMe), 3.6—4.5 (7-H, 16-H, and 20-H_2), and 4.50 (1 H, t, J 8 Hz, 6-H) (Found: M^+, 378.202. Calc. for $C_{21}H_{30}O_6$ requires M, 378.204), and was identical (i.r. and n.m.r. spectra and behaviour on t.l.c.) with an authentic sample. *ent*-3β,20:6β,19-Diepoxy-7α,19-dihydroxy-3,16α-dimethoxy-17-norkaurane (16) (amorphous) showed δ 1.14 (3 H, s, 4-Me), 3.30 (6 H, s, 2 × OMe), 3.6—4.4 (6-, 7-, and 16-H, and 20-H_2), and 5.82 (1 H, s, 19-H); the diacetate (amorphous) showed δ 1.13 (3 H, s, 4-Me), 2.10 and 2.12 (each 3 H, s, 2 × OAc), 3.28 and 3.33 (each 3 H, s, 2 × OMe), *ca.* 3.7 (1 H, m, 16-H), 3.83 and 4.62br (each 1 H, AB-type, J 10 Hz, 20-H_2), 4.15 (1 H, t, J 4 Hz, 6-H), 5.20 (1 H, d, J 4 Hz, 7-H), and 6.73 (1 H, s, 19-H).

Jones Oxidation of the Diacetate of the Diol (16).—To a solution of the diacetate (8 mg) in acetone (1 ml) was added Jones reagent (1 drop) with stirring at room temperature. After 15 min, a small amount of isopropyl alcohol was added, and the mixture was extracted with dichloromethane. The usual treatment of the extract gave a crystalline product (5.5 mg), which was recrystallised from methanol to give *ent*-7α-acetoxy-3β,20-epoxy-3,16α-dimethoxy-17-norkauran-19,6β-olide as needles, m.p. 286—288° (decomp.), $\nu_{max.}$ 1 772, 1 738, 1 230, and 1 062 cm^{-1}, 1.33 (3 H, s, 4-Me), 2.07 (3 H, s, OAc), 3.27 and 3.41 (each 3 H, s, 2 × OMe), 3.5—4.5 (16-H and 20-H_2), 4.43 (1 H, t, J 6 Hz, 6-H), and 5.42 (1 H, d, J 6 Hz, 7-H), identical with the acetate of (9) (i.r., m.p., and t.l.c.).

Reaction of the Epoxy-lactone (22) *with Boron Trifluoride–Ether.*—To a stirred solution of the epoxy-lactone (22) (228 mg) in dichloromethane (19 ml) and methanol (1 ml) were added a few drops of boron trifluoride–ether at room temperature. After 15 min, dichloromethane (200 ml) was added and the mixture was washed with water. The organic layer was dried and evaporated and the crystalline residue was recrystallised (MeOH–$CHCl_3$) to separate two products. The major product, ent-3β,20-*epoxy*-7α-*hydroxy*-3,6α,16α-*trimethoxy*-17-*norkauran*-19,6-*olide* (24) was obtained as needles (62%), m.p. 207—209° (from MeOH), $\nu_{max.}$ ($CHCl_3$) 3 550, 1 782, and 1 072 cm^{-1}, δ 1.50 (3 H, s, 4-Me), 3.30, 3.40, and 3.46 (each 3 H, s, 3 × OMe), *ca.* 3.80 (1 H, m, 16-H), 3.93 (1 H, s, 7-H), and 3.86 and 4.32 [each 1 H, AB-type, J 10 Hz, 20-H_2; lower field signal showed long-range coupling with 1β-H (J 3 Hz)] (Found: M^+, 408.212. $C_{22}H_{32}O_7$ requires M, 408.214). The acetate was amorphous, δ 1.46 (3 H, s, 4-Me), 2.12 (3 H, s, OAc), 3.28 (3 H, s, OMe), 3.43 (6 H, s, 2 × OMe), 3.6—4.0 (16-H and one proton of 20-H_2), 4.40 [1 H, one part of AB type, J 10 Hz, 20-H; this signal showed long-range coupling (J 3 Hz)], and 5.48 (1 H, s, 7-H) (Found: M^+, 450.228. $C_{24}H_{34}O_8$ requires M, 450.225).

The minor product, ent-3β,20-*epoxy*-6α-*fluoro*-7α-*hydroxy*-3,16α-*dimethoxy*-17-*norkauran*-19,6-*olide*, was obtained as needles (26%), m.p. 230° (from MeOH), $\nu_{max.}$ 3 400, 1 800, 1 100, and 1 010 cm^{-1}, δ 1.48 (3 H, s, 4-Me), 3.31 and 3.42 (each 3 H, s, 2 × OMe), 3.6—4.1 (7-H, 16-H, and one proton of 20-H_2), and 4.23 (1 H, one part of AB-type, J 10 and 3 Hz, 20-H; also long-range coupling with 1β-H) (Found: C, 63.7; H, 7.55. $C_{21}H_{29}FO_6$ requires C, 63.6; H, 7.35%).

The *acetate* was obtained as prisms, m.p. 215° (decomp.) (from MeOH), $\nu_{max.}$ 1 800, 1 745, 1 230, and 1 015 cm^{-1}, δ 1.47 (3 H, s, 4-Me), 2.15 (3 H, s, OAc), 3.25 and 3.42 (each 3 H, s, 2 × OMe), *ca.* 3.80 (1 H, m, 16-H), 3.90 and 4.32 [each 1 H, AB type, *J* 10 Hz, 20-H_2; each signal showed long-range coupling (*J* 1 and 3 Hz, respectively)], and 5.44 (1 H, d, *J* 12 Hz, 7-H) (Found: M^+, 438.205. $C_{23}H_{31}FO_7$ requires *M*, 438.205).

Conversion of the Alcohol (24) *into its Epimer* (26).—To a stirred solution of the alcohol (24) (65 mg) in dichloromethane (10 ml) was added Collins reagent (300 mg) at 0 °C. After 1 h, a black deposit was filtered off and the filtrate on column chromatography (SiO_2; CH_2Cl_2) gave ent-3β,20-*epoxy*-3,6α,16α-*trimethoxy*-7-*oxo*-17-*norkauran*-19,6-*olide* (25) (53 mg) as leaflets, m.p. 236—237° (from MeOH), $\nu_{max.}$ 1 785, 1 710, and 1 043 cm^{-1}, δ 1.42 (3 H, s, 4-Me), 3.30, 3.34, and 3.37 (each 3 H, s, 3 × OMe), and 3.50—4.10 (16-H, 20-H_2) (Found: C, 64.7; H, 7.75. $C_{22}H_{30}O_7$ requires C, 65.0; H, 7.45%). To a solution of this ketone (25) (36 mg) in methanol (10 ml) was added sodium borohydride (23 mg) at room temperature, and the mixture was stirred. After 15 min, the mixture was extracted with dichloromethane and the extract treated as usual to give a crystalline product (35 mg), which was recrystallised from methanol to give ent-3α,20-*epoxy*-7β-*hydroxy*-3,6α,16α-*trimethoxy*-17-*norkauran*-19,6-*olide* (26) (26 mg) as prisms, m.p. 152—157°, $\nu_{max.}$ 3 300, 3 200, 1 783, and 1 030 cm^{-1}, δ 1.47 (3 H, s, 4-Me), *ca.* 2.20 (1 H, OH), 3.30, 3.40, and 3.47 (each 3 H, s, 3 × OMe), 3.6—4.1 (16-H and one proton of 20-H_2), and 4.90 (1 H, AB type, *J* 10 and 3 Hz, 20-H) (Found: C, 61.8; H, 8.45. $C_{22}H_{32}O_7,H_2O$ requires C, 61.95; H, 8.05%).

ent-3β,20-*Epoxy*-3,6α,16α-*trimethoxy*-7β-*methylsulphonyloxy*-17-*norkauran*-19,6-*olide* (23).—A solution of the alcohol (26) (29 mg) and methanesulphonyl chloride (5 drops) in pyridine (2 ml) was kept overnight at room temperature. The mixture was poured into dilute hydrochloric acid with cooling (ice) and extracted with dichloromethane. The usual work-up gave a gum, which was chromatographed (SiO_2; CH_2Cl_2) to separate the amorphous methanesulphonate (23) (20 mg), δ 1.40 (3 H, s, 4-Me), 3.23 (3 H, s, OMs), 3.26, 3.36, and 3.44 (each 3 H, s, 3 × OMe), 3.73 and 4.54 [each 1 H, AB-type, *J* 10 Hz, 20-H_2; lower field signal showed long-range coupling (*J* 3 Hz)], *ca.* 3.90 (1 H, m, 16-H), and 4.82 (1 H, s, 7-H); M^+ 486.

Reaction of the Epoxy-lactone (22) *with Lithium Bromide.*—To a solution of hexamethylphosphoric triamide (1 ml) in benzene (1 ml) was added lithium bromide (62 mg), and the mixture was refluxed for 15 min under nitrogen. Subsequently, the epoxy-lactone (22) [2] (10 mg) was added. After 1 h under reflux, extraction with benzene and treatment as usual gave a mixture, which was chromatographed (SiO_2; CH_2Cl_2) to separate the amorphous ent-3β,20-*epoxy*-3,16α-*dimethoxy*-6-*oxo*-17,19-*bisnorkaur*-4-*ene* (27) (3.5 mg, 40%), $\nu_{max.}$ 1 765, 1 685, and 1 050 cm^{-1}, $\lambda_{max.}$ 250 nm (ε 6 900), δ 2.33 (3 H, s, 4-Me), 3.33 and 3.46 (each 3 H, s, 2 × OMe), 3.6—4.1 (16- and 20-H), and 4.03 (1 H, one part of AB type, *J* 8 Hz, 20-H) (Found: M^+, 332.202. $C_{20}H_{28}O_4$ requires *M*, 332.198).

Reaction of the Methanesulphonate (23) *with Potassium Hydroxide.*—Potassium hydroxide (50 mg) in water (0.5 ml) was added to a solution of the methanesulphonate (23) (19 mg) in t-butyl alcohol (2 ml) and the mixture was boiled for 5 h in a stream of nitrogen. Addition of water, acidification (dil. HCl), and extraction (CH_2Cl_2) gave a gum which was chromatographed (SiO_2; CH_2Cl_2) to separate an αβ-unsaturated ketone (9 mg, 70%), identical (i.r. and n.m.r. spectra) with (27).

This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, which is gratefully acknowledged. We also thank Mrs. J. Tanaka of this Institute for mass spectral determinations.

[6/361 *Received*, 23*rd February*, 1976]