Fluorinated Kaurenoids. Part 2.[1] Preparation of Methyl *ent*-17,17,17-Trifluorokaur-15-en-19-oate and *ent*-16,16-Difluoro-17-norkauran-19-oic Acid from Xylopic Acid

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An attempt to convert methyl *ent*-16-oxo-17-norkauran-19-oate (3), derived from xylopic acid, into methyl *ent*-17,17-difluorokaur-16-en-19-oate failed. However, treatment of the norketone (3) with diethylaminosulphur trifluoride (DAST) gave methyl *ent*-16,16-difluoro-17-norkauran-19-oate (5). The latter afforded the corresponding acid (4) which was active as a growth promoter in a dwarf-rice bioassay. Treatment of methyl deacetylxylopate (18) with DAST, followed by cleavage of the terminal methylene group, yielded methyl *ent*-15-fluoro-16-oxo-17-norkauran-19-oate (15), which on reaction with dibromodifluoromethane and tris(dimethylamino)phosphine gave, not the expected 17,17-difluoro-olefin (19), but methyl *ent*-17,17,17-trifluorokaur-15-en-19-oate (28) in poor yield. Reduction of methyl xylopate with di-imide gave the 16β-methyl compound (24) stereospecifically. The latter was readily converted into methyl 15-oxokauranoate (26), but steric hindrance prevented the reaction of the oxo-group with DAST to give the 15,15-difluoride, under normal reaction conditions; using a much longer reaction time a trace of the *gem*-difluoride was formed.

During reduction of the dithiocarbonate (27) of methyl deacetylxylopate with tri-n-butyltin hydride into the isomeric methyl kaurenoates (8) and (31), the 17-thiol ester (32) was also formed by a [3,3]sigmatropic rearrangement.

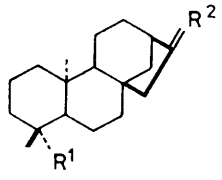
THE preparation of fluorinated analogues of the precursors in the biosynthesis of the gibberellins and their use in the production of otherwise inaccessible fluorogibberellins and as enzyme inhibitors has been reported.[1-4]

At low concentration the difluorokaurene (1) had no detectable effect on a *Gibberella fujikuroi* fermentation, but preliminary results showed that it inhibited [1,5] the oxidation of *ent*-kaurene in a cell-free enzyme system which biosynthesised gibberellins. The difluoro-acid (2) is the analogue of a later intermediate on the biosynthetic pathway to the gibberellins [6] and might show higher biological activity [*cf.* the *ent*-fluorokaurene (9) [1] and *ent*-fluorokaurenoic acid (10)].[3]

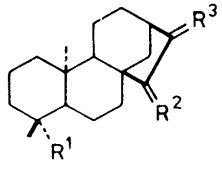
The preparation of the difluoro-acid (2) was attempted from the norketone (3), which was derived from xylopic acid (11) [7] by the reaction sequence shown in the Scheme. On one occasion the diol (12) was obtained as a by-product.

One experiment in which the norketone ester (3) was treated with dibromodifluoromethane and tris(dimethylamino)phosphine [1,8] failed to give identifiable products and use of the norketone (3) was abandoned in favour of the more readily available fluoro-ketone (15). The latter was prepared from deacetylxylopic acid (16),[7] which was first methylated and then fluorinated with diethylaminosulphur trifluoride (DAST) [9] at 0 °C for 5 min, to give the fluoro-olefin (17).

Fluorination of methyl deacetyloxylopate (18) with 2-chloro-*NN*-diethyl-1,1,2-trifluoroethylamine afforded the same fluoro-olefin (17) (*cf.* ref. 1). Hence the fluorine atom in the latter was assigned the α-configuration.[1,2] Cleavage of the terminal methylene group in the olefin (17), with osmium tetraoxide–sodium periodate, afforded the required ketone (15) which only reacted with dibromodifluoromethane and tris(dimethylamino)phosphine with difficulty. However, using an excess of the aminophosphine as solvent the reaction yielded a product which was a trifluoro-ester, $C_{21}H_{29}F_3O_2$, the ^{19}F n.m.r.

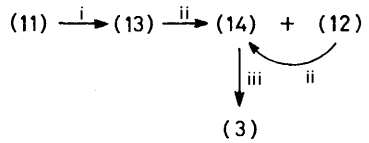


	R^1	R^2
(1)	Me	CF_2
(2)	CO_2H	CF_2
(3)	CO_2Me	O
(4)	CO_2H	F_2
(5)	CO_2Me	F_2
(6)	CH_2OH	F_2
(7)	CO_2H	CH_2
(8)	CO_2Me	CH_2



	R^1	R^2	R^3
(9)	Me	α-F, β-H	CH_2
(10)	CO_2H	α-F, β-H	CH_2
(11)	CO_2H	α-H, β-OAc	CH_2
(12)	CO_2Me	α-H, β-OAc	α-OH, β-CH_2OH
(13)	CO_2Me	α-H, β-OAc	CH_2
(14)	CO_2Me	α-H, β-OAc	O
(15)	CO_2Me	α-F, β-H	O
(16)	CO_2H	α-H, β-OH	CH_2
(17)	CO_2Me	α-F, β-H	CH_2
(18)	CO_2Me	α-H, β-OH	CH_2
(19)	CO_2Me	α-F, β-H	CF_2
(20)	CO_2H	α-F, β-H	CF_2
(21)	CO_2H	α-F, β-H	O
(22)	$CONMe_2$	α-F, β-H	O
(23)	CO_2H	F_2	α-H, β-Me
(24)	CO_2Me	α-H, β-OAc	α-H, β-Me
(25)	CO_2Me	α-H, β-OH	α-H, β-Me
(26)	CO_2Me	O	α-H, β-Me
(27)	CO_2Me	α-H, β-OCS_2Me	CH_2

spectrum of which showed only one signal as a singlet at ϕ* 67.25; this was consistent with the presence of a $=C-CF_3$ group, as in structure (28). Confirmation was



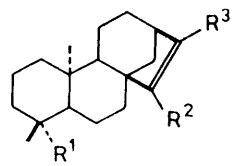
SCHEME *Reagents:* i, CH_2N_2; ii, OsO_4–$NaIO_4$; iii, Ca–liquid NH_3

provided by its ^1H n.m.r. spectrum which showed only one olefinic proton as a multiplet at δ 6.01. The latter was assigned to the 15-proton shifted downfield by the trifluoromethyl group [in the n.m.r. spectrum of isokaurene (29) the 15-proton signal occurs at δ 5.07]. Structure (28) is assumed to arise by allylic rearrangement of the trifluoride (19).

An attempt to prepare the 17,17-difluoro-acid (20) by replacing the oxo-ester (15), in the above 'difluoro-Wittig' reaction, with the oxo-acid (21), afforded the oxo-amide (22) in good yield; this reaction may be a convenient method of converting acids into amides.

The difluoro-acid (4) was prepared as a potential enzyme inhibitor in the following manner. Treatment of the oxo-ester (3) with DAST in carbon tetrachloride in a bomb at 114 °C (*cf.* ref. 10) gave the difluoro-ester (5), which was reduced with lithium aluminium hydride to the alcohol (6). Oxidation of the latter with Jones reagent afforded the difluoro-acid (4).

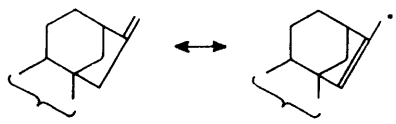
The acid (4) was considerably more active than *ent*-kaurene, but less active than *ent*-kaurenoic acid (7) in the Tanginbozu-rice bioassay.[11] The results of further biological assays will be reported.



	R^1	R^2	R^3
(28)	CO_2Me	H	CF_3
(29)	Me	H	Me
(30)	CO_2Me	$O{\cdot}CS_2Me$	Me
(31)	CO_2Me	H	Me
(32)	CO_2Me	H	$CH_2{\cdot}S{\cdot}CO{\cdot}SMe$

An attempt to prepare the 15,15-difluoro-acid (23) was made as follows. Methyl xylopate (13) was reduced with di-imide (*cf.* refs. 10, 12) to give the 16β-epimer of the dihydro-ester (24). Hydrolysis of the acetyl group gave the alcohol (25), which was oxidised to the ketone (26) with Jones reagent. However, attempts to fluorinate the ketone with DAST afforded either unchanged material or, under forcing conditions, black, intractable gums, indicating the hindered nature of the 15-oxo-group. Reduction of the gums with lithium aluminium hydride, followed by oxidation with Jones reagent, gave a trace of the 15,15-difluoro-acid (23).

Kaurenoic acid (7) is a valuable intermediate in the preparation of fluoro-analogues of the biosynthetic precursors of the gibberellins. An attempt was made to prepare it from deacetylxylopic acid [7] by removal of the 15-hydroxy-group by Barton's dithiocarbonate reduction.[13] Treatment of the alcohol (18) with carbon disulphide, sodium hydride, and methyl iodide yielded the required dithiocarbonate (27) (58%) [δ 6.19 (dd, J 2 Hz, 15-H), 5.00 (17-H_2), and 2.61 (SMe)]. The n.m.r. spectrum of a second isomeric dithiocarbonate, formed in 28% yield, contained no low-field signals, but showed methyl singlets at δ 1.48 (C=C–Me) and 2.61 (SMe) and was assigned the structure (30). Reduction of the dithiocarbonate (27) with tri-n-butyltin hydride gave methyl kaurenoate (8) and its isomer (31) in almost equal amounts (g.l.c. analysis), presumably because the reduction proceeds *via* the resonance stabilised radical (33). A third and minor product was found to be the rearranged compound (32) which presumably arises by a



(33)

[3,3]sigmatropic shift. Its n.m.r spectrum showed signals at δ 5.39 (m, 15-H), 3.77 (m, 17-H_2), 2.50 (m, 13-H), and 2.45 (SMe). In agreement, its mass spectrum showed a molecular ion and an ion at *m/e* 347 (M — S·CO·SMe). Support for the structure of the thiol ester (32) was provided by the observation that it was formed exclusively on heating the dithiocarbonate (27) in toluene.

EXPERIMENTAL

Details of chromatographic materials and conditions used for determination of physical data, *etc.*, have been reported.[2,14]

Methyl ent-15α-*Acetoxy*-16-*oxo*-17-*norkauran*-19-*oate* (14).—Methyl xylopate (13) [7] (1.123 g) in dioxan (50 ml) and acetic acid (12 ml) was treated with osmium tetraoxide (100 mg) in dioxan (10 ml). After 10 min, sodium metaperiodate (1.3 g) was added and the mixture stirred for 5 h. Sodium metabisulphite (*ca.* 5 g) and pyridine (10 ml) were added and the mixture was stirred for a further 1 h. The products were recovered in chloroform and the *norketone* (14) crystallised from methanol as prisms (708 mg, 63%), m.p. 177—178 °C (Found: C, 70.3; H, 8.5. $C_{22}H_{32}O_5$ requires C, 70.2; H, 8.6%); $\nu_{max.}$ 1 763, 1 747, 1 720, 1 238, and 1 225 cm^{-1}; δ 4.89 (1 H, s, 15-H), 3.56 (3 H, s, OMe), 2.54 (m, $w_{\frac{1}{2}}$ 10 Hz, 13-H), 2.20 (3 H, s, COMe), 1.20 (3 H, s, 18-H_3), and 0.93 (3 H, s, 20-H_3).

Purification of the mother liquors from the crystallisation of the norketone (14), by preparative t.l.c. (development in chloroform) afforded a band at R_F 0.1—0.2 which contained *methyl* ent-15α-*acetoxy*-16β,17-*dihydroxykauran*-19-*oate* (12) (16%) which crystallised from carbon tetrachloride–light petroleum, m.p. 137—139 °C (Found: C, 67.9; H, 8.9. $C_{23}H_{36}O_6$ requires C, 67.6; H, 8.9%); $\nu_{max.}$ 3 400br, 1 750, 1 734, 1 721, and 1 239 cm^{-1}; δ 4.71 (1 H, s, 15-H), 3.66

(3 H, s, OMe), 2.12 (3 H, s, COMe), 1.16 (3 H, s, 18-H_3), and 0.86 (3 H, s, 20-H_3).

Periodate Oxidation of the Diol (12).—The diol (150 mg) in tetrahydrofuran (THF) (5 ml) and water (1 ml) was treated with sodium metaperiodate (500 mg) for 5 min. Recovery in chloroform gave the norketone (14) (102 mg), identical (n.m.r. spectrum) with the sample prepared above.

Methyl ent-16-*Oxo*-17-*norkauran*-19-*oate* (3).—The norketone (14) (600 mg) in THF (30 ml) was added, as drops during 10 min, to calcium (1.02 g) in anhydrous ammonia (70 ml) and THF (15 ml) and the mixture was stirred for 30 min. The products were recovered in chloroform and the solution was evaporated to give a gum which was dissolved in acetone (20 ml), cooled to 0 °C, and treated with an excess of Jones reagent for 30 min. The mixture was diluted with sodium metabisulphite solution and the products were extracted with chloroform to afford a gum. Preparative t.l.c. in chloroform gave *methyl* ent-16-*oxo*-17-*norkauran*-19-*oate* (3) (353 mg, 70%) as a band at R_F 0.3—0.5; it crystallised from methanol as plates, m.p. 170—171 °C (Found: *m/e*, 318.219 3. $C_{20}H_{30}O_3$ requires *M*, 318.219 5); $\nu_{max.}$ 1 743 and 1 723 cm^{-1}; δ 3.66 (3 H, s, OMe), 1.96 (2 H, s, 15-H_2), 1.20 (3 H, s, 18-H_3), and 0.91 (3 H, s, 20-H_3); *m/e* 318, 286, 259, and 258.

Reduction of the ester (3) (85 mg) with lithium aluminium hydride (80 mg) in ether at 20 °C for 25 h and recovery in ethyl acetate gave a solid. Oxidation of the latter with Jones reagent at 20 °C for 2 h and recovery in ethyl acetate yielded *ent*-16-oxo-17-norkauranoic acid (82 mg), which crystallised from ethyl acetate–light petroleum, identical (n.m.r. spectrum) with an authentic sample.[15]

Attempted Preparation of Methyl 17,17-*Difluorokaur*-16-*en*-19-*oate*.—Treatment of the norketone (3) in triglyme with dibromodifluoromethane and tris(dimethylamino)-phosphine, as for 17-norkaur-16-one,[1] gave intractable gums.

Methyl ent-15β-*Fluorokaur*-16-*en*-19-*oate* (17).—The hydroxy-ester (18) (166 mg) in dry dichloromethane (2 ml) was cooled to 0 °C, DAST (0.1 ml) was added, and the mixture was stirred for 5 min. Water was added and the product was recovered in chloroform to give an oil which was purified by preparative t.l.c. [development in chloroform–light petroleum (3 : 7)]. Material obtained from the band of R_F 0.3—0.5 afforded the *fluoro-ester* (17) (134 mg, 80%) which crystallised from methanol in needles, m.p. 107—109 °C (Found: C, 75.3; H, 9.5; F, 5.7. $C_{21}H_{31}FO_2$ requires C, 75.4; H, 9.3; F, 5.7%); $\nu_{max.}$ 1 730, 1 715, 921, and 910 cm^{-1}; δ 5.27 (2 H, m, 17-H_2), 4.45 (1 H, d, J_{HF} 56 Hz, 15-H), 3.66 (3 H, s, OMe), 2.84 (1 H, m, 13-H), 1.19 (3 H, s, 18-H_3), and 0.84 (3 H, s, 20-H_3).

Methyl ent-15β-*Fluoro*-16-*oxo*-17-*norkauran*-19-*oate* (15).—The fluoro-ester (17) (1.17 g) was treated with osmium tetraoxide and sodium metaperiodate, as for the 15-acetoxy-analogue (see above), and the products were chromatographed on silica gel (60 g). Elution with ethyl acetate–light petroleum (1 : 9) gave the *fluoro-norketone* (15) (730 mg, 62%) which crystallised from ethanol as plates, m.p. 166—169 °C (Found: C, 71.4; H, 8.8; F, 6.8%; *m/e*, 336.210 7. $C_{20}H_{29}FO_3$ requires C, 71.4; H, 8.7; F, 5.6%; *M*, 336.210 1); $\nu_{max.}$ 1 761, 1 729, and 997 cm^{-1}; δ 4.07 (1 H, dd, J_{HF} 50 and *J* 2.5 Hz, 15-H), 3.68 (3 H, s, OMe), 2.61 (1 H, m, 13-H), 1.22 (3 H, s, 18-H_3), and 0.93 (3 H, s, 20-H_3); ϕ* 202.06 (d, J_{HF} 52 Hz); *m/e* 336, 321, 316, 305, and 277.

Methyl ent-17,17,17-*Trifluorokaur*-15-*en*-19-*oate* (28).—Tris(dimethylamino)phosphine (10 ml) was cooled to 0 °C under nitrogen and dibromodifluoromethane (0.75 ml) was added slowly to give a white slurry, which was stirred while the fluoro-norketone (15) (190 mg), suspended in the aminophosphine (5 ml), was added. Stirring was continued for a further 63 h and water was added, followed by ether. The ethereal layer was washed several times with dilute perchloric acid, dried, and evaporated to give a gummy solid. Purification by preparative t.l.c. [development with chloroform–light petroleum (1 : 3)] afforded a band at R_F 0.5 from which the *trifluoro-ester* (28) (58 mg) was recovered with acetone; it crystallised from methanol (Found: *m/e*, 370.210 5. $C_{21}H_{29}F_3O_2$ requires *M*, 370.211 9); $\nu_{max.}$ 1 722, 1 650, 1 278, 1 141, and 887 cm^{-1}; δ 6.01 (1 H, m, $w_{\frac{1}{2}}$ 6 Hz, 15-H), 3.63 (3 H, s, OMe), 2.81 (1 H, $w_{\frac{1}{2}}$ 20 Hz, 13-H), 1.15 (3 H, s, 18-H_3), and 0.85 (3 H, s, 20-H_3); ϕ* 67.25; *m/e* 370, 355, 350, 311, 310, and 295.

Reaction of the Oxo-acid (21) *with Tris(dimethylamino)-phosphine and Dibromodifluoromethane*.—Dibromodifluoromethane (1 g) was added to the oxo-acid (75 mg) in tris-(dimethylamino)phosphine (10 ml). The reaction was at first exothermic; later it was stirred for 28 h at room temperature and then diluted with ethyl acetate and 2M-hydrochloric acid. Recovery of the ethyl acetate layer gave the 15α-*fluoro*-NN-*dimethyl*-16-*oxo*-17-*norkauran*-19-*amide* (22) as a gum (80 mg) (Found: *m/e*, 349.241 7. $C_{21}H_{32}FNO_2$ requires *M*, 349.241 9); δ 4.04 (1 H, dd, J_{HF} 51 and *J* 2 Hz, 15-H), 3.03 (6 H, s, NMe_2), 2.60 (1 H, m, 13-H), 1.29 (3 H, s, 18-H_3), and 1.04 (3 H, s, 20-H_3); *m/e* 349, 334, 329, 322, 278, and 277.

Fluorination of Methyl ent-16-*Oxo*-17-*norkauran*-19-*oate* (3).—The oxo-ester (3) (550 mg) in dry carbon tetrachloride (10 ml) was treated with DAST (1.8 ml) in a bomb at 114 °C for 72 h. The mixture was poured into water and the products were extracted into carbon tetrachloride. Evaporation under reduced pressure and purification of the residue by preparative t.l.c. (development in benzene), afforded *methyl* ent-16,16-*difluoro*-17-*norkauran*-19-*oate* (5) (316 mg) which crystallised from light petroleum, m.p. 107—108 °C (Found: C, 70.05; H, 9.2%; *m/e*, 340.222 5. $C_{20}H_{30}F_2O_2$ requires C, 70.6; H, 8.9%; *M*, 340.221 4); $\nu_{max.}$ ($CHCl_3$) 1 718, 1 160, 1 110, and 990 cm^{-1}; δ 3.64 (3 H, s, OMe), 1.18 (3 H, s, 18-H_3), and 0.85 (3 H, s, 20-H_3); ϕ* 109.47 (dm, *J* 230 Hz, 16-F) and 84.68 (2 × dd, *J* *ca.* 225 and 16 Hz, 16-F); *m/e* 340, 320, 300, 281, 261, and 246.

Reduction of the Difluoro-ester (5) *with Lithium Aluminium Hydride*.—The ester (5) (300 mg) in ether (15 ml) was treated with lithium aluminium hydride (600 mg) at room temperature for 24 h. Isolation of the product in the usual way, followed by crystallisation from light petroleum gave ent-16,16-*difluoro*-17-*norkauran*-19-*ol* (6) as prisms (244 mg), m.p. 118—119 °C (Found: C, 73.3; H, 9.7; F, 12.3. $C_{19}H_{30}F_2O$ requires C, 73.0; H, 9.6; F, 12.2%); $\nu_{max.}$ ($CHCl_3$) 3 450, 1 450, 1 370, 1 350, and 1 110 cm^{-1}; δ 3.67 (2 H, dd, *J* 11 Hz, 19-H_2), 1.01 (3 H, s, 18-H_3), and 0.94 (3 H, s, 20-H_3); *m/e* 312, 292, 282, 281, 272, and 261.

ent-16,16-*Difluoro*-17-*norkauran*-19-*oic Acid* (4).—The alcohol (6) (198 mg) in acetone (15 ml) was treated with Jones reagent (2 ml) at room temperature for 1 h. Recovery in ethyl acetate and crystallisation from light petroleum gave needles of the *difluoronorkauranoic acid* (4), m.p. 195—196 °C (Found: C, 69.8; H, 8.65. $C_{19}H_{28}F_2O_2$ requires C, 69.9; H, 8.6%); $\nu_{max.}$ 3 300—2 500, 1 695, 1 175, and 1 110 cm^{-1}; δ 0.95 (3 H, s, 20-H_3) and 1.22 (3 H, s, 18-H_3); *m/e* 326 (*M*), 306, 286, 282, and 281.

Reduction of Methyl Xylopate (13) *with Di-imide*.—Methyl

xylopate (1.6 g) in ethanol (50 ml) was treated with hydrazine hydrate (4 ml) at 0 °C. Hydrogen peroxide (30%; 4 ml) was added during 1 h after which the mixture was stirred at 0 °C for 3 h and then at room temperature for 12 h. Ethanol was removed under reduced pressure and the mixture was acidified with dilute hydrochloric acid. Recovery in ethyl acetate gave nearly pure methyl *ent*-15α-acetoxykauran-19-oate (24) (1.1 g), δ 0.82 (3 H, d, *J* 7 Hz, 17-H_3), 0.85 (3 H, s, 20-H_3), 1.15 (3 H, s, 18-H_3), 2.1 (3 H, s, OAc) 3.61 (3 H, s, OMe), and 4.77 (1 H, d, *J* 7 Hz, 15-H), which was used in the following experiment.

Methyl ent-15α-*Hydroxykauran*-19-*oate* (25).—The acetate (24) (1.1 g) in methanol (40 ml) was refluxed with 2M-potassium hydroxide (30 ml) for 2 h. The solution was acidified with dilute hydrochloric acid and the product was recovered in ethyl acetate. Evaporation under reduced pressure gave *methyl* ent-15α-*hydroxykauran*-19-*oate* (25) (920 mg) which crystallised from ethyl acetate (Found: *m/e*, 334.249 0. $C_{21}H_{34}O_3$ requires *M*, 334.250 8); δ 0.84 (3 H, s, 20-H_3), 0.94 (3 H, d, *J* 7 Hz, 17-H_3), 1.15 (3 H, s, 18-H_3), 3.61 (3 H, s, OMe), and 3.58 (1 H, d, br, 15-H); *m/e* 334, 319, 316, and 275.

Methyl ent-15-*Oxokauran*-19-*oate* (26).—The hydroxy-ester (25) (900 mg) in acetone (50 ml) was treated with Jones reagent for 3 h at room temperature. Recovery in ethyl acetate and crystallisation from n-hexane gave needles of the *oxo-ester* (26) (850 mg), m.p. 106—107 °C (Found: *m/e*, 332.235 0. $C_{21}H_{32}O_3$ requires *M*, 332.235 1); $\nu_{max.}$ ($CHCl_3$) 1 730 cm^{-1}; δ 0.88 (3 H, s, 20-H_3), 1.05 (3 H, d, *J* 7 Hz, 17-H_3), 1.16 (3 H, s, 18-H_3), and 3.61 (3 H, s, OMe); *m/e* 332, 317, 304, 289, and 274; pure by g.l.c.

Fluorination of Methyl ent-15-*Oxokauran*-19-*oate* (26) *with DAST*.—(a) *For 6 d*. The oxo-ester (26) (100 mg) in dry carbon tetrachloride (10 ml) was treated with DAST in a bomb at 114 °C for 6 d. The mixture was poured into water, extracted with carbon tetrachloride, the extract was dried over potassium carbonate, and the solvent was removed under reduced pressure to give a gum, shown by t.l.c. and mass spectroscopy to consist mainly of the starting ketone.

(b) *For 13 d*. The oxo-ester (716 mg) in carbon tetrachloride (12 ml) was heated in a bomb with DAST (2.7 ml) at 114 °C for 13 d. Work-up in the usual way gave a black gum, which after column and preparative thin layer chromatography (the latter developed with benzene), afforded an intractable gum.

The gum was reduced with an excess of lithium aluminium hydride in ether for 24 h and the crude product was oxidised with an excess of Jones reagent in the usual way. The acidic product was purified by preparative t.l.c. (developed in ethyl acetate–light petroleum × 2) and gave two main bands. Material from the slower running band yielded 15-oxokauran-19-oic acid identical (i.r. and n.m.r. spectra) with an authentic sample.[7]

Material from the faster running band gave 15,15-*difluorokauran*-19-*oic acid* (23) as a gum (5 mg) (Found: *m/e*, 340.221 8. $C_{20}H_{30}F_2O_2$ requires *M*, 340.221 4); δ 1.00 (3 H, s, 20-H_3), 1.09 (3 H, d, *J* 7 Hz, 17-H_3), and 1.25 (3 H, s, 18-H_3).

Preparation of the Dithiocarbonate (27) *of Methyl* ent-15α-*Hydroxykaur*-16-*en*-19-*oate* (18).—Methyl deacetylxylopate (18) (665 mg) and imidazole (5 mg) in THF (20 ml) were treated with sodium hydride (125 mg) and the mixture was refluxed under nitrogen for 2 h; carbon disulphide (0.7 ml) was then added and heating was continued for 30 min. Methyl iodide (1 ml) was then added and the solution heated for a further 15 min. Glacial acetic acid (2 ml) and water were added and the mixture was extracted with chloroform. Recovery gave an oil which was separated by preparative t.l.c. [development in chloroform–light petroleum (3 : 7)] into two major bands. Material recovered from the band at R_F 0.5 gave O-(ent-4β-*methoxycarbonylkaur*-16-*en*-15-*yl*) S-*methyl dithiocarbonate* (27) as a pale yellow oil, (490 mg, 58%); $\nu_{max.}$ (film) 1 725, 1 487, 1 217, 1 144, and 1 062 cm^{-1}; δ 6.19 (1 H, t, J_{15-17} 2 Hz, 15-H), 5.00 (2 H, m, $w_{\frac{1}{2}}$ 10 Hz, 17-H_2), 3.65 (3 H, s, OMe), 2.74 (1 H, m, $w_{\frac{1}{2}}$ 10 Hz, 13-H), 2.61 (3 H, s, SMe), 1.16 (3 H, s, 18-H_3), and 0.87 (3 H, s, 20-H_3). Irradiation at the frequency of the terminal methylene group caused the signal at δ 6.19 to collapse to a singlet (Found: *m/e*, 422.195 3; C, 65.1; H, 7.9; S, 14.9%. $C_{23}H_{34}O_3S_2$ requires *M*, 422.194 9; C, 65.4; H, 8.1; S, 15.2%); *m/e* 422, 362, 315, and 255.

Material from the band at R_F 0.4 gave the isomeric O-(ent-4β-*methoxycarbonylkaur*-15-*en*-15-*yl*) S-*methyl dithiocarbonate* (30) of methyl *ent*-17-hydroxykaur-15-en-19-oate (236 mg; 28%) which crystallised from ethanol as amber prisms, m.p. 189—190 °C (Found: *m/e*, 422·194 5; C, 65·3; H, 8.0; S, 15.4%. $C_{23}H_{34}O_3S_2$ requires *M*, 422.194 9; C, 65.4; H, 8.1; S, 15.2%); $\nu_{max.}$ 1 744, 1 724, 1 233, 1 161, and 942 cm^{-1}; (in $CHCl_3$) 1 720 and 1 159 cm^{-1}; δ 3.64 (3 H, s, OMe), 3.19 (1 H, m, $w_{\frac{1}{2}}$ 8 Hz, 13-H), 2.61 (3 H, s, SMe), 2.22 (1 H, d, *J* 14 Hz, 14β-H?), 1.48 (3 H, s, 17-H_3), 1.18 (3 H, s, 18-H_3), and 0.87 (3 H, s, 20-H_3); *m/e* 422, 407, 394, 389, 379, and 375.

Reduction of the Dithiocarbonate (27) *with Tri-n-butyltin Hydride*.—The dithiocarbonate (400 mg) was added during 1 h to tri-n-butyltin hydride (956 mg) in dry toluene (20 ml) which was heated under reflux in an atmosphere of nitrogen; heating was continued for 2 h and then the toluene was evaporated under reduced pressure. Purification of the product by preparative t.l.c. [development with chloroform–light petroleum (3 : 7)] gave bands at R_F 0.4 and 0.5.

Recovery of material from the band of higher R_F gave an oil (268 mg; 89%) which was shown by g.l.c. to contain only methyl kaur-16-en-19-oate (49%) and methyl kaur-15-en-19-oate (51%).

Material from the band at R_F 0.4 gave S-(ent-4β-*methoxycarbonylkaur*-15-*en*-17-*yl*) S-*methyl dithiocarbonate* (32) (40 mg; 10%) as an oil (Found: *m/e*, 422.194 0. $C_{23}H_{34}O_3S_2$ requires *M*, 422.194 9); $\nu_{max.}$ (film) 1 725, 1 646 (S.CO.S), 1 231, 1 158, and 869 cm^{-1}; δ 5.39 (1 H, m, $w_{\frac{1}{2}}$ 4 Hz, 15-H), 3.77 (2 H, s, 17-H_2), 3.66 (3 H, s, OMe), 2.50 (1 H, m, $w_{\frac{1}{2}}$ 10 Hz, 13-H), 2.45 (3 H, s, SMe), 1.17 (3 H, s, 18-H_3), and 0.86 (3 H, s, 20-H_3); *m/e* 422, 362, 347, and 255.

Rearrangement of the Dithiocarbonate (27).—The dithiocarbonate (45 mg) in toluene (5 ml) was heated under reflux for 2.5 h. Evaporation of the solvent under reduced pressure gave, as the sole product, the 17-thio-derivative (32), identical (i.r. and n.m.r. spectra) with the sample prepared in the previous experiment.

We thank the S.R.C. for a research grant and Miss M. B. Burbage (Tropical Products Institute) for the supply of *Xylopia aethiopica*.

[0/1184 *Received*, 28*th July*, 1980]

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