Conjugate Addition of Lithium Methylcuprates to a Gibberell-1(10)en-2-one; Preparation of 10-*epi*-Gibberellin A_{53}

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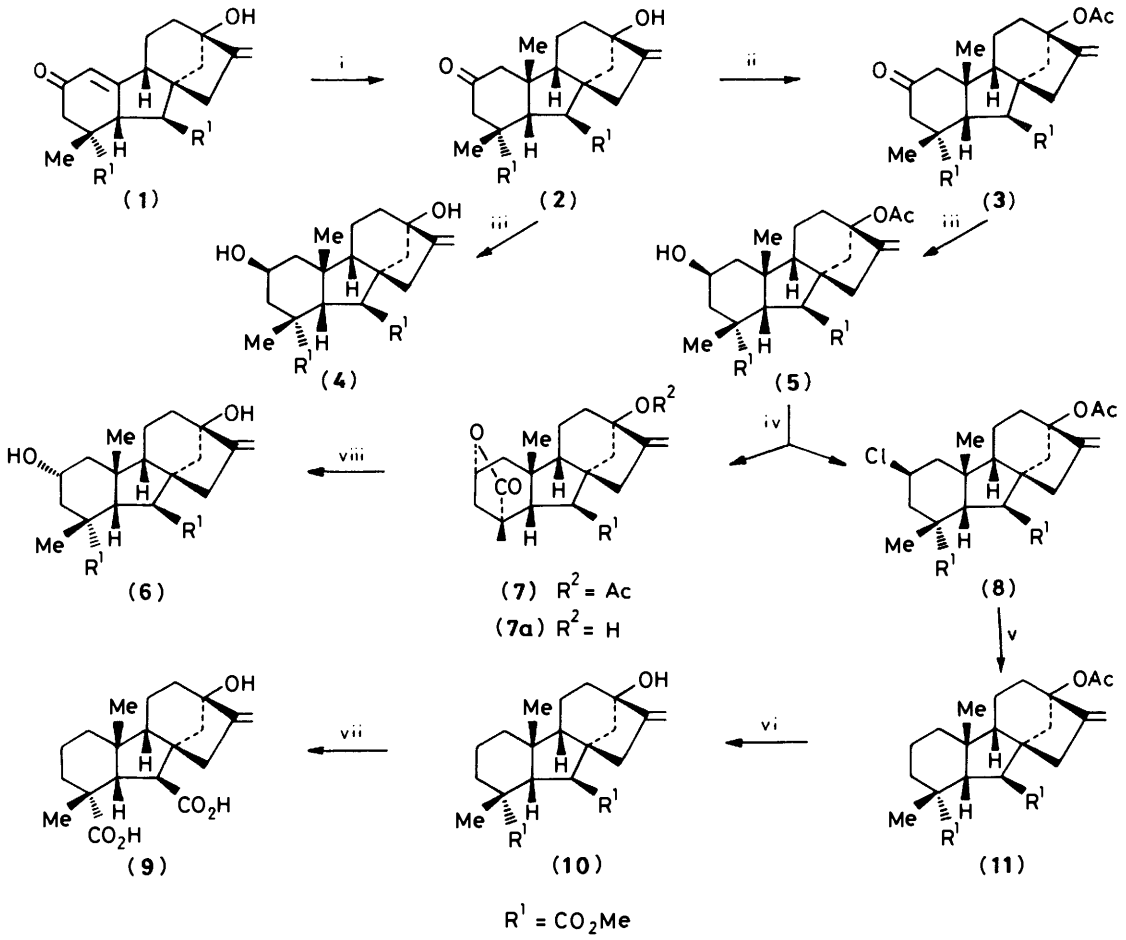
The conjugate addition of a methyl group by $Li_2Cu_3Me_5$ to the known enone (**1**) is described. The stereochemistry of this alkylation was determined by ^1H n.m.r. experiments. The product (**2**) was converted in six steps into 10-*epi*-gibberellin A_{53} (**9**).

As a continuation of our programme concerned with the conversion of the available fungal gibberellins (GAs) such as gibberellin A_3 (**12**) into the rare, higher plant gibberellins and bioactive analogues we have examined the conjugate addition of lithium methylcuprates to the enone (**1**) (Scheme) in the hope that addition from the α-face at C-10 in (**1**) would provide entry into synthetic routes from C_{19} to C_{20} gibberellins such as GA_{53} (**13**) and GA_{19} (**14**). In the event, addition occurred from the β-face providing intermediates for the synthesis of 10-*epi*-C_{20} gibberellins. Compounds belonging to the 10-*epi* series have not been prepared previously. It was hoped that they might show activity as plant growth regulators as a result of inhibition of the enzyme(s) concerned with the conversion of the C_{20} into the C_{19} gibberellins.

Results and Discussion

The enone (**1**) was prepared from gibberellin A_3 (**12**) in five steps by a known route.[1] Initial alkylation experiments using lithium dimethylcuprate prepared from methyl-lithium and either cuprous iodide or cuprous bromide–dimethyl sulphide complex[2] in ether–tetrahydrofuran were not encouraging. The reactions were sluggish and the product contained mainly the epimeric 9-hydroxy-ketones (**15**). Thorough deoxygenation of the solvents prevented the formation of (**15**) but enolisation to C-9 remained a problem and the required conjugate addition product (**2**) (Scheme) was always contaminated with the deconjugated ketone (**16**) which co-chromatographed with (**2**).

Better results were obtained with the more reactive[3,4] pentamethyl cuprate, $Li_2Cu_3Me_5$. Although the reaction was



Scheme. *Reagents:* i, $Li_2Cu_3Me_5$; ii, Ac_2O, TsOH; iii, $NaBH_4$; iv, $POCl_3$, py; v, Bu_3SnH; vi, K_2CO_3; vii, PrSNa, HMPA; viii, NaOMe

never complete, treatment of (**1**) with $Li_2Cu_3Me_5$ in ether at 0 °C ⟶ 20 °C gave, cleanly, a single 10-methyl ketone (**2**) in 42% isolated yield based on recovered starting material (see Scheme). Reduction of this ketone with sodium borohydride in ethanol yielded a single alcohol (**4**) in quantitative yield. The magnitude of the coupling constants of 2-H (quint, *J* 3.5 Hz) in the ^{1}H n.m.r. of (**4**) indicated that the alcohol group was in an axial position. The signals for the C-4β and C-10 methyl groups in (**4**) occurred at δ 1.38 and 1.64 respectively. Their positions in the starting ketone (**2**) were δ 1.34 and 1.2 (see Table). The significant downfield shift of the C-10 methyl group indicates that it is *cis*-1,3-diaxial to the 2-alcohol. Examination of molecular models showed that attack of borohydride on the ketone (**2**) could occur from the α-face if the methyl group at C-10 is in the β position and ring A was in a boat conformation. The C-4β methyl group in (**4**) is also 1,3-disposed to the C-2-hydroxy function, but is not shifted downfield from its position in (**2**) and thus appears to be in an equatorial position. This leads to the boat conformation for ring-A in the alcohol (**4**) as shown in the Figure. As is typical in the ^{1}H n.m.r. of gibberellins

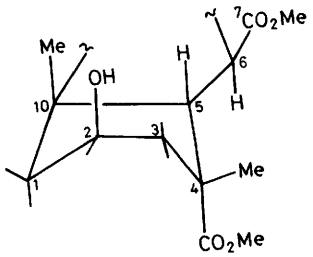


Figure.

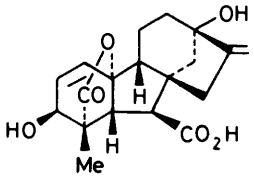
the doublets (*J* 11 Hz) for 5β-H and 6α-H were apparent at δ 2.38 and 2.85 respectively. N.O.e. difference spectra were obtained for irradiation at 2α-H, 5β-H, and 6α-H. The C-4β and C-10 methyl signals were equally enhanced when 5β-H was irradiated. No enhancement was observed when 2α-H or 6α-H were irradiated. Thus the 4β- and 10-methyls are both on the same side of the molecule as 5β-H confirming both the above stereochemical assignments and that the initial conjugate addition had occurred from the β-face.

Acetylation of (**2**) to give (**3**) followed by borohydride reduction gave the 13-protected 2β-alcohol (**5**) as a single compound in near quantitative yield which on treatment with phosphoryl chloride in pyridine gave two products. The major product (52% yield) was a chloride, assigned the 2β-stereochemistry (**8**) by virtue of the downfield shift of the 10β-methyl group (to δ 1.58) which suggests the same boat conformation for ring A as in the alcohol (**4**).

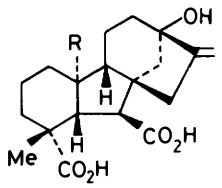
The more polar product (22% yield) was identified as the 19⟶2 lactone (**7**). Analysis of the ^{1}H n.m.r. spectrum of (**7**) in conjunction with molecular models indicates a chair conformation resulting in a reduced 5-H to 6-H coupling constant (3 Hz) and close proximity of the 19-carbonyl function to the 14α-proton the signal for which appears downfield at δ 2.71 as a doublet of triplets (*J* 15,3 Hz). The formation of the lactone from the 2β-alcohol was unexpected, but is not without precedent. Beeley and MacMillan [5] have reported the lactonisation of GA_{46} methyl ester (**20**) on treatment with toluene-*p*-sulphonic acid in refluxing benzene. To confirm the stereochemical assignments made above for the 2β-alcohols (**4**) and (**5**) the lactone (**7**) was treated with sodium methoxide in methanol to give the 2α-alcohol (**6**) the ^{1}H n.m.r. spectrum of which (see Table) was very different from that of (**4**). In particular, the 10β-methyl group signal appeared at δ 1.19, well upfield of its position in the 2β-alcohol (**4**) (δ 1.64) and the signal for the 2β-

Table. ^{1}H N.m.r. ($CDCl_3$) of 10-*epi*-gibberellanes

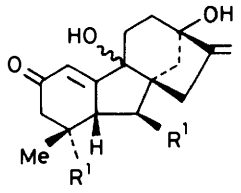
Compd.	10-Me	4-Me	2-H	5-H	6-H
(**2**)	1.20	1.34		2.56 (*J* 8)	3.02 (*J* 8)
(**4**)	1.64	1.39	4.38 (quint. *J* 3)	2.38 (*J* 11)	2.86 (*J* 11)
(**8**)	1.58	1.42	4.71 (dd, *J* 6,3)	2.36 (*J* 10)	2.88 (*J* 10)
(**7**)	1.20	1.31	4.85 (t, *J* 5)	2.39 (*J* 3)	2.98 (*J* 3)
(**6**)	1.19	1.44	3.97 (tt, *J* 11,4)	2.27 (*J* 11)	3.02 (*J* 11)
(**10**)	1.12	1.38		2.24 (*J* 10)	2.96 (*J* 10)
(**17**)	1.14	1.42			
(**18**)	1.21	1.29			



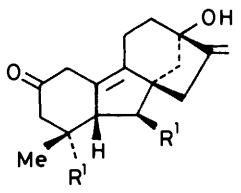
(**12**)



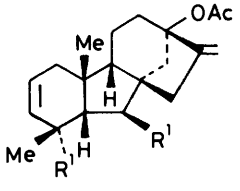
(**13**) GA_{53} R = Me
(**14**) GA_{19} R = CHO



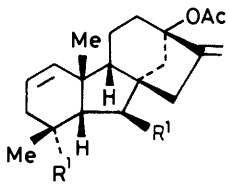
(**15**)



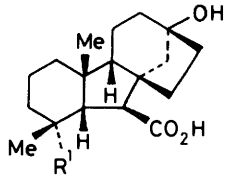
(**16**)



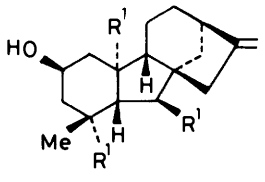
(**17**)



(**18**)



(**19**)



(**20**)

$R^1 = CO_2Me$

carbinol proton occurred at δ 3.97 as a triplet of triplets (*J* 11 and 4 Hz). The magnitude of these coupling constants indicates that the 2α-hydroxy group is in an equatorial position and that ring-A again is in the boat conformation proposed for the β-alcohol above.

Reduction of the chloride (**8**) with tributylstannane gave the 10-*epi*-GA_{53}-acetate dimethyl ester (**11**) which was shown to be contaminated with 16% of two olefins in the ratio 4:1 by capillary g.c.–mass spectrometry. Reversed-phase preparative h.p.l.c. gave pure (**11**) but failed to separate the two olefins. However comparison, by g.l.c. and ^{1}H n.m.r., of the olefin mixture with the 2,3-olefin (**17**) prepared by a different route[7] revealed that the major isomer was the 1,2-olefin (**18**) and the minor isomer was the 2,3-olefin (**17**)

Hydrolysis of the acetate dimethyl ester (**11**) with sodium hydroxide in dioxane–water was incomplete and gave mainly the 13-hydroxy 19-methyl ester (**19**). Therefore (**11**) was treated first with potassium carbonate–methanol to give the 13-hydroxy diester (**10**) and then hydrolysed with sodium propanethiolate in hexamethylphosphoramide to give 10-*epi*-GA_{53} (**9**). Direct comparison of (**9**) with authentic GA_{53} (**13**) by capillary g.c.–mass spectrometry of their Me_2SiMe_3 derivatives showed them to be isomers with different g.c. retention times.

10-*epi*-GA_{53} was recovered unchanged after incubation for 3 days with the mutant B1-41a of *Gibberella fujikuroi*. Preliminary bioassay results on the d_5 dwarf and tall maize systems indicate that (**9**) is devoid of any plant growth regulatory activity.

Experimental

For general details see ref. 6.

ent-13-*Hydroxy*-2-*oxo*-10α-*gibberell*-16-*ene*-7,19-*dioic Acid* 7,19-*Dimethyl Ester* (**2**).—A solution of $Li_2Cu_3Me_5$ was prepared by the addition of methyl-lithium (1.4M ether solution; 14.5 ml, 20.2 mmol) to a suspension of cuprous iodide (2.3 g, 12.15 mmol) in dry deoxygenated ether (30 ml) with stirring under nitrogen.

This solution was cooled to 0 °C while the enone (**1**) (0.90 g, 2.4 mmol) in dry deoxygenated ether–tetrahydrofuran (10:1; 25 ml) was added dropwise with stirring during 10 min. The cooling bath was removed and the reaction mixture stirred for 5 h and then cautiously added to dilute hydrochloric acid–ice with stirring. The product was extracted into ethyl acetate. Flocculent copper salts were removed from the recovered organic layer by addition of anhydrous sodium sulphate and filtration through a sinter. Evaporation of the ethyl acetate gave a gum which was purified by stepped, flash chromatography on a 16 × 3 cm column eluted with the following percentages of ethyl acetate in light petroleum: 30% (200 ml), 40% (300 ml), 50% (300 ml), 60% (300 ml), and 70% (100 ml) in 20-ml fractions.

Fractions 31—42 gave the 10β-methyl 2-ketone (**2**) (311 mg), m.p. 133—134 °C (acetone–light petroleum) (Found: C, 67.9; H, 7.8. $C_{22}H_{30}O_6$ requires C, 67.67; H, 7.74%); $\nu_{max.}$ 3 500, 1 735, 1 712, 1 665, and 895 cm^{-1}; δ($CDCl_3$) 1.20 (3 H, s, 10-Me), 1.34 (3 H, s, 4-Me), 2.56 (1 H, d, *J* 8, 5-H), 2.6 (1 H, d, *J* 15, 1-H or 3-H), 2.88 (1 H, d, *J* 15, 1-H or 3-H), 3.02 (1 H, d, *J* 8, 6-H), 3.64 and 3.71 (6 H, s, 2 × CO_2Me), 4.94 and 5.18 (2 H, 2 × br s, 17-H_2); ^{13}C δ($CDCl_3$) 210.2 (s, C-2), 175.6 and 174.3 (2 s, C-7 and C-19), 155.1 (s, C-16), 106.2 (t, C-17), 78.4 (s, C-13), 55.2, 54.9, and 53.6 (3 d, C-5, -6, and -9), 52.2 and 51.5 (2 q, 2 × OMe), 48.5, 47.2, and 46.9 (3 s, C-4, -8, and -10), 46.4, 45.6, and 45.6 (3 t, C-1, -3, and -15), 43.0 (t, C-14), 38.4 (t, C-12), 31.1 and 25.7 (2 q, C-18 and C-20), and 18.1 (t, C-11); *m/z* 390 (*M*$^+$, 6%), 375 (8), 372 (4), 358 (98), 330 (100), 315 (46), 299 (25), 298 (25), 288 (18), 271 (26), 255 (23), 135 (21), and 123 (21).

Fractions 46—56 gave the starting enone (**1**) (164 mg).

ent-2α,13-*Dihydroxy*-10α-*gibberell*-16-*ene*-7,19-*dioic Acid* 7,19-*Dimethyl Ester* (**4**).—The 10β-methyl 2-ketone (**2**) (40 mg) in ethanol (2 ml) was treated with sodium borohydride (30 mg) for 1—5 h at room temperature. Addition of water, acidification to pH 3 with dilute hydrochloric acid, and recovery in ethyl acetate gave a gum. Removal of residual boron compounds by p.l.c. on silica gel (ethyl acetate–light petroleum, 3:2) gave the pure 2β-alcohol (**4**) (40 mg) (Found: *M*$^+$ − 32, 360.1938; *M*$^+$ − 60, 332.1980. $C_{21}H_{28}O_5$ requires *M* − CH_3OH, 360.1936; $C_{20}H_{28}O_4$ requires *M* − CH_3CO_2H, 332.1987); δ($CDCl_3$) 1.38 (3 H, s, 4-Me), 1.64 (3 H, s, 10-Me), 2.38 (1 H, d, *J* H, 5-H), 2.85 (1 H, d, *J* 11, 6-H), 3.57 and 3.64 (6 H, 2 s, 2 × CO_2Me), 4.36 (1 H, quint, *J* 3.5 Hz, 2-H), and 4.81 and 5.14 (2 H, 2 br, s, 17-H_2); *m/z* 392 (*M*$^+$, 2%), 374 (1), 360 (100), 332 (89), 317 (26), 314 (31), 300 (20), 299 (25), 282 (13), 272 (29), 260 (12), 255 (16), and 107 (12).

ent-13-*Acetoxy*-2-*oxo*-10α-*gibberell*-16-*ene*-7,19-*dioic Acid* 7,19-*Dimethyl Ester* (**3**).—The 10β-methyl 2-ketone (**2**) (60 mg) was treated with acetic anhydride (1 ml) and toluene-*p*-sulphonic acid (1 crystal) for 2 h at room temperature. The solution was then taken up in ethyl acetate and washed with saturated aqueous sodium hydrogen carbonate and then water. Evaporation gave the 13-acetate (**3**) (63 mg) as a gum (Found: *M*$^+$, 432.2141. $C_{24}H_{32}O_7$ requires *M*$^+$, 432.2148); δ($CDCl_3$) 1.17 (3 H, s, 10-Me), 1.34 (3 H, s, 4-Me), 1.98 (3 H, s, OCOMe), 2.52 (2 H, d, *J* 10, 5-H), 2.56 (1 H, d, *J* 15, 1-H or 3-H), 2.92 (1 H, d, *J* 15, 1-H or 3-H), 3.16 (1 H, d, *J* 10, 6-H), 3.58 and 3.68 (6 H, 2 s, 2 × CO_2Me), and 4.89 and 5.02 (2 H, 2 × br s, 17-H_2); *m/z* 432 (*M*$^+$, 21%), 400 (24), 390 (25), 372 (29), 357 (16), 340 (100), 330 (20), 312 (28), 297 (13), 229 (19), 123 (12), and 43 (31).

ent-13-*Acetoxy*-2α-*hydroxy*-10α-*gibberell*-16-*ene*-7,19-*dioic Acid* 7,19-*Dimethyl Ester* (**5**).—The keto acetate (**3**) (63 mg) in ethanol (2 ml) was treated with sodium borohydride (50 mg) for 2 h at room temperature. After work-up, the product was recovered in ethyl acetate and separated from residual boron compounds by p.l.c. on silica gel (ethyl acetate–light petroleum, 1:1) to give the 2β-alcohol (**5**) (59 mg) (Found: *M*$^+$ − 32, 402.2020. $C_{23}H_{30}O_6$ requires *M* − MeOH, 402.2042); δ($CDCl_3$) 1.39 (3 H, s, 4-Me), 1.65 (3 H, s, 10-Me), 2.02 (3 H, s, OCOMe), 2.36 (1 H, d, *J* 12, 5-H), 2.90 (1 H, d, *J* 12, 6-H), 3.56 and 3.64 (6 H, 2 s, 2 × CO_2Me), 4.37 (1 H, br, $w_{\frac{1}{2}}$ 12 Hz, 2-H), and 4.90 and 5.09 (2 H, 2 × br s, 17-H_2); *m/z* 434 (*M*$^+$, 3%), 416 (2), 402 (70), 374 (69), 359 (16), 342 (31), 314 (100), 299 (18), 255 (10), 237 (10), and 43 (21).

ent-13-*Acetoxy*-2α-*chloro*-10α-*gibberell*-16-*ene*-7,19-*dioic Acid* 7,19-*Dimethyl Ester* (**8**).—The alcohol (**5**) (90 mg) in dry pyridine (4 ml) and phosphorus oxychloride (300 μl) was stirred at room temperature for 20 min and then heated under reflux for 1.5 h. The solvent was then evaporated under a stream of nitrogen and the residue subjected to p.l.c. on silica gel (ethyl acetate–light petroleum, 4:6) to give at higher R_F the chloride (**8**) (47 mg) (Found: *M*$^+$, 452.1945; *M*$^+$ − 32, 420.1719. $C_{24}H_{33}{}^{35}ClO_6$ requires *M*$^+$, 452.1965; $C_{23}H_{29}{}^{35}ClO_5$ requires *M* − CH_3OH, 420.1703); δ($CDCl_3$) 1.42 (3 H, s, 4-Me), 1.58 (3 H, s, 10-Me), 2.02 (3 H, s, OCOMe), 2.37 (1 H, d, *J* 10, 5-H), 2.58 (1 H, dd, *J* 15, 5.5, 1-H or 3-H), 2.88 (1 H, d, *J* 10, 6-H), 3.59 and 3.66 (6 H, 2 s, 2 × CO_2Me), 4.71 (1 H, dq, *J* 6, 3, 2-H), and 4.93 and 5.08 (2 H, 2 × br s, 17-H_2); *m/z* 452 (*M*$^+$, 9%), 420/422 (100/36), 392/394 (65/24), 384 (26), 377/379 (22/9), 360/362 (37/13), 356 (36), 332/334 (78/34), 317/319 (28/12), 297 (25), 296 (22), 273 (20), 237 (14), 185 (14), 143 (21), 107 (30), and 43 (41).

The band at lower R_F gave the lactone (**7**) (20 mg) (Found: *M*$^+$, 402.2050. $C_{23}H_{30}O_6$ requires *M*$^+$, 402.2042); δ 1.20 (3 H, s, 10-Me), 1.3 (3 H, s, 4-Me), 2.00 (3 H, s, OCOMe), 2.39 (1 H, d, *J* 3, 5-H), 2.71 (1 H, d t, *J* 15, 3, 14α-H), 2.98 (1 H, d, *J* 3, 6-H), 3.69 (3 H, s, CO_2Me), 4.85 (1 H, t, *J* 3, 2-H), and 4.94 (2 H, br s, 17-

H_2); *m/z* 402 (M^+, 17%), 360 (30), 342 (19), 328 (9), 310 (100), 300 (6), 295 (13), 282 (11), 268 (6), 229 (12), and 43 (11).

Treatment of the Lactone (**7**) *with Sodium Methoxide.*—The lactone (**7**) (12 mg) in 2M-sodium methoxide in methanol (5 ml) was refluxed overnight. After evaporation of the solvent the residue was partitioned between dilute hydrochloric acid and ethyl acetate. The organic layer was treated with diazomethane and evaporated to give a gum which was chromatographed on a short column of silica gel (8 × 2 cm) eluted with ethyl acetate–light petroleum (1:1; 50 ml), ethyl acetate (50 ml), and acetone (30 ml) in 10 13-ml fractions. Fraction 4 (5 mg) contained the 13-hydroxy-lactone (**7a**), δ($CDCl_3$) 1.20 (3 H, s, 10-Me), 1.31 (3 H, s, 4-Me), 2.40 (1 H, d, *J* 3, 5-H), 2.59 (1 H, dt, *J* 16,3, 14-H), 2.95 (1 H, d, *J* 3, 6-H), 3.69 (3 H, s, CO_2Me), 4.84 (1 H, t, *J* 3, 2-H), and 4.93 and 5.12 (2 H, 2 × br, s, 17-H_2); *m/z* 360 (M^+, 54%), 328 (100), 300 (55), 187 (27), 163 (30), 135 (33), 105 (32), and 91 (40). Fractions 7 and 8 (5.5 mg) contained the 2α-alcohol (**6**), δ($CDCl_3$ + D_2O) 1.19 (3 H, s, 10-Me), 1.44 (3 H, s, 4-Me), 2.27 (1 H, d, *J* 11, 5-H), 3.02 (1 H, d, *J* 11, 6-H), 3.58 and 3.65 (6 H, 2 s, 2 × CO_2Me), 3.97 (1 H, tt, *J* 11, 4, 2-H), and 4.88 and 5.16 (2 H, 2 × br s, 17-H_2); *m/z* 374 (*M* − 18, 4%), 360 (66), 342 (28), 328 (75), 314 (100), 300 (86), 282 (27), 255 (44), 208 (32), 187 (27), 163 (25), 137 (39), and 135 (32).

ent-13-*Acetoxy*-10α-*gibberell*-16-*ene*-7,19-*dioic Acid* 7,19-*Dimethyl Ester* (**11**).—The 2β-chloride (**8**) (47 mg) in benzene (5 ml) with 2,2′-Dimethyl-2,2′-azopropionitrile (1 mg) and tri-n-butylstannane (200 μl) were refluxed for 2 h. The solvent was then evaporated and tin residues were removed by p.l.c. on silica gel (50% acetone in light petroleum) to give the crude 10-*epi*-GA_{53} dimethyl ester acetate (**11**) (51 mg) containing by g.c.–mass spectrometry the 1,2-olefin (**18**) (13%) and the 2,3-olefin (**17**) (3%).

Final purification was achieved by preparative h.p.l.c. on a 25 cm × 8 mm i.d. 5 μ Hypersil ODS column with 70% methanol, 30% water at 3 ml/min and u.v. detection at 210 nm. Injections of 3—4 mg were made. Retention times: mixed olefins R_t 22 min and 10-*epi*-GA_{53} dimethyl ester acetate R_t 28 min. The relevant fractions from h.p.l.c. were evaporated and then extracted with ethyl acetate to give pure 10-epi-GA_{53} *dimethyl ester acetate* (**11**) (30 mg) (Found: M^+ − 32, 386.2040. $C_{23}H_{30}O_5$ requires M^+ − CH_3OH 386.2093); δ($CDCl_3$), 1.14 (3 H, s, 1-Me), 1.41 (3 H, s, 4-Me), 2.02 (3 H, s, OCOMe), 2.53 (1 H, d, *J* 12, 5-H), 3.077 (1 H, d, *J* 12, 6-H), 3.55 and 3.64 (6 H, 2 s, 2 × CO_2Me), and 4.90 and 5.09 (2 H, 2 × br s, 17-H_2); *m/z* 386 (M^+ − 32, 5%), 359 (19), 343 (13), 326 (8), 316 (12), 248 (100), 283 (18), 239 (18), 238 (14), 183 (5), and 109 (10).

The olefinic material (5 mg) (*m/z* 384, M^+ − 32) was a 4:1 mixture by n.m.r. spectrometry. Major component (**18**) δ 1.21 and 1.29 (6 H, 2 s, 2 × Me), 1.99 (3 H, s, 3.59 and 3.67 (6 H, 2 s, 2 × CO_2Me), 4.94 (2 H, br, 17-H_2), and 5.68 (2 H, m, 1-H and 2-H). Minor component (**17**) δ 1.14 and 1.42 (6 H, 2 s, 2 × Me), 2.02 (3 H, s, OCOMe), 3.56 and 3.64 (6 H, 2 s, 2 × CO_2Me), and 4.94 and 5.10 (2 H, 2 × br s, 17-H_2), and 5.68 (2 H, m, 2-H and 3-H).

ent-13-*Hydroxy*-10α-*gibberell*-16-*ene*-7,19-*dioic Acid* (**9**).—The acetate dimethyl ester (**11**) (20 mg) in methanol (1.5 ml) and water (0.5 ml) with potassium carbonate (100 mg) were stirred overnight. The mixture was then diluted with water, acidified to pH 3 and extracted with ethyl acetate to give the alcohol–dimethyl ester (**10**) (20 mg) (Found: M^+ − 32, 344.2006. $C_{21}H_{28}O_4$ requires *M* − CH_3OH, 344.1987); δ($CDCl_3$) 1.12 (3 H, s, 10-Me), 1.38 (3 H, s, 4-Me), 2.24 (1 H, d, *J* 10, 5-H), 2.96 (1 H, d, *J* 10, 6-H), 3.48 and 3.59 (6 H, 2 s, 2 × CO_2Me), and 4.80 and 5.05 (2 H, 2 × br s, 17-H_2).

The above dimethyl ester (20 mg) was treated with the supernatant solution (10 ml) prepared from hexamethylphosphoramide (15 ml), sodium hydride (1 g of 50% oil dispersion, washed with light petroleum) and propanethiol (1 ml) in the normal way.[6] After 4 h at room temperature the solution was left at 0 °C overnight and then added to water (50 ml). The water was washed with ethyl acetate and then acidified to pH 3 with dilute hydrochloric acid and extracted with ethyl acetate to yield an oil. This oil was adsorbed onto a short column of silica gel. After elution of non-polar material with 20% ethyl acetate in light petroleum, the product was eluted with 80—100% ethyl acetate. Final purification was by flash chromatography on a 16 × 1 cm column eluted with ethyl acetate–light petroleum–acetic acid (80:20:1) (100 ml) and then ethyl acetate–acetic acid (100:1) (100 ml) in 10-ml fractions. Fractions 6—11 gave pure 10-*epi*-GA_{53} (**9**) (8.5 mg); *m/z* (tris $SiMe_3$ derivative) 564 (M^+, 50%), 549 (62), 474 (28), 447 (38), 446 (38), 328 (45), 309 (12), 239 (18), 235 (20), and 207 (55) and identical to starting dimethyl ester when treated with diazomethane.

G.l.c.–Mass Spectrometric Comparison with GA_{53} (**13**).—As Me_2, $SiMe_3$ derivatives on a 25 m × 0.2 mm flexible silica WCOT column (OV1, 0.25 μm) with He carrier at 2 bar. Injections (with alkane standards) were made at ambient temperature and programmed at 13 °C/min to 150 °C and then 3 °C/min to 300 °C.

Kovats retention indices (KRI's)10-*epi*-GA_{53} Me_2,$SiMe_3$ = 2 545, GA_{53} Me_2,$SiMe_3$ = 2 492.

Acknowledgements

I am indebted to Professor J. MacMillan for helpful advice and discussions; Professor B. O. Phinney (U.C.L.A.) for the use of the fungal mutant B1-41a and for conducting the bioassay; and Dr. M. Murray for the n.O.e. experiment.

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Received 24*th September* 1984; *Paper* 4/1638