Two Efficient Partial Syntheses of Gibberellin A_{81} from Gibberellin A_3

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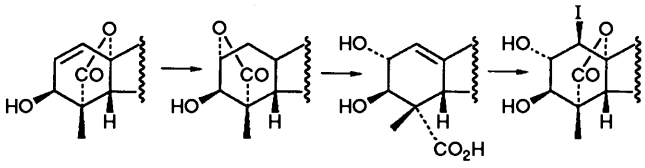
Two efficient routes for the synthesis of gibberellin A_{81} (2-*epi*-gibberellin A_{29}) from gibberellin A_3 are described. Both methods employ strategies based on iodolactonisation procedures and avoid manipulation of rings C/D.

2-*epi*-Gibberellin A_{29} (2-*epi*-GA_{29}) **1** has been reported to occur in extracts of *Pisum sativum*,[1] *Lathyrus odorata*,[2] *Citrus sinensis*[3] and other sources (unpublished). Identification was based on GLC–MS comparison of the methylated and trimethylsilylated natural product and the bis-trimethylsilyl ether of the methyl ester **2**, prepared[4,5] in the course of the synthesis of GA_{29} **3**. Because of its presence in plant extracts, 2-*epi*-GA_{29} **1** is now assigned[6] the GA-number, GA_{81}.

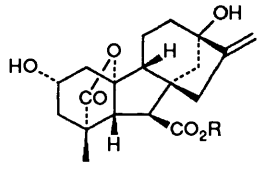
In this paper we describe, in full, two efficient partial syntheses of GA_{81} **1** from GA_3 **4**. They are shown in Schemes 2 and 4 and are described later. One of these routes (Scheme 2) has been reported in preliminary form.[7] Both routes employ strategies that transform the ring A functionality of GA_3 **4** into that of GA_{81} **1** without protection or manipulation of rings C and D. The key reaction sequence (Scheme 1) is the conversion of GA_3 **4** into the iodo triol **5** by the hydrolysis–iodo lactonisation procedure described by Corey *et al.*[8] As shown in Scheme 1 the sequence proceeds *via* base-catalysed rearrangement of GA_3 **4** to the isomeric 19,2-lactone,[9] followed by lactone hydrolysis then regeneration of the 19,10-lactone by iodo lactonisation. The sequence can be performed either step-wise or in a one-pot reaction.

Based on the reaction sequence of Scheme 1, the initial approach comprised an attempt to prepare the 3-deoxy analogue **6** of the iodo triol **5** and hence by reductive deiodination of **6** to prepare GA_{81} methyl ester **2**. However

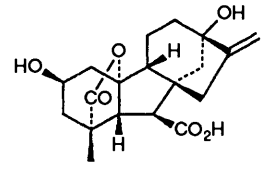


Scheme 1

this potentially economic route was abandoned when attempted 3-deoxygenation of GA_3 isomeric 19,2-lactone methyl ester **7** *via* the 3-*S*-methyl xanthate **8** failed. Treatment of the isolactone **7** with potassium hydride and carbon disulphide, followed by methyl iodide, did not give the expected product **8** but a mixture of the cyclic dithiocarbonate **9** and the trienoic acid **10**. The same products were also formed when methyl iodide was omitted from the reaction mixture. The formation of **10** can be rationalised by an intramolecular S_N2' attack of the intermediate 3β-dithiocarbonate anion at C-2 of the allylic lactone. The trienoic acid **10** appears to be formed by decomposition of **9**. Indeed treatment of **9** with tributylstannane and radical initiator results in formation of **10**, together with a separable isomer, assigned structure **11** from the UV (λ_{max}/nm 247), ^1H ^{13}C NMR spectra. Slow formation of the heteroannular diene **11** was also observed when solutions of **10** in dichloromethane or chloroform were allowed to stand at room temp. for several days. Although the original approach to the



1 R = H
2 R = Me



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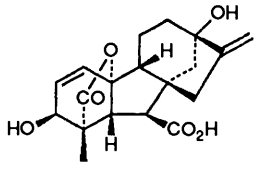

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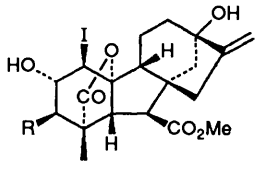
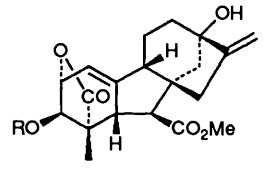
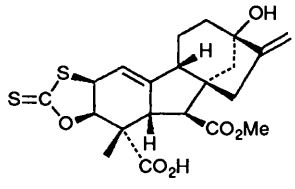


5 R = OH
6 R = H



7 R = H
8 R = MeSCS



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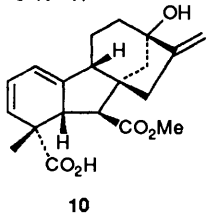

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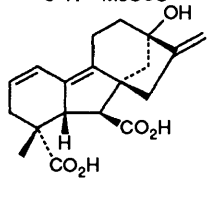

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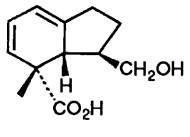

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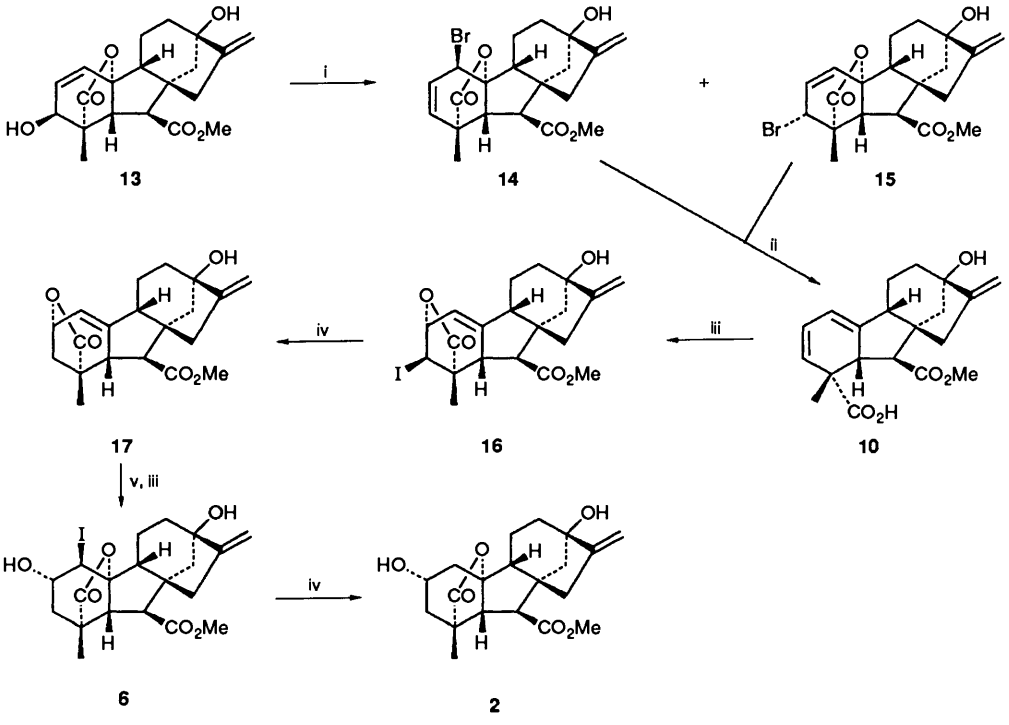
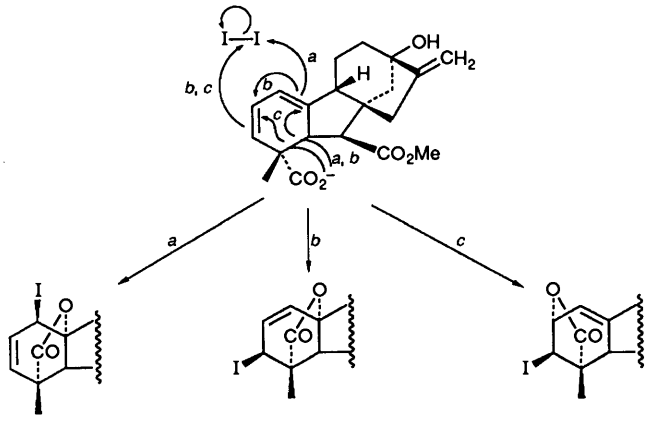


Scheme 2 *Reagents:* i, CBr_4, PPh_3; ii, Zn, AcOH; iii, aq.$NaHCO_3$, I_2, CH_2Cl_2, THF (tetrahydrofuran); iv, Bu_3SnH; v, 0.5 mol dm^{-3} KOH

partial synthesis of GA_{81} **1** was unsuccessful, a successful route to GA_{81} **1** was developed from the trienoic acid **10** as described in the next section.

Route 1 (*Scheme* 2).—A superior route to the required trienoic acid **10** comprised treatment of GA_3 methyl ester **13** with carbon tetrabromide and triphenylphosphine in refluxing acetone containing pyridine. In our hands (*cf.* ref. 10) this reaction gave a mixture (3:1) of the 1β- and 3α-allylic bromides **14** and **15**. Reduction of the mixture with activated zinc and acetic acid in ethyl acetate gave the trienoic acid **10** in 78% overall yield from GA_3 methyl ester **13**. Treatment of the trienoic acid **10** with sodium hydrogen carbonate and iodine in a biphasic solvent system of tetrahydrofuran, dichloromethane and water (1:1:2) yielded a single iodo lactone **16**. The structure **16** was deduced from the ^1H NMR spectrum which contained only the olefinic proton signal at δ 5.82, assigned to 1-H, in addition to the exocyclic methylene proton signals. The structure **16** was supported by a triplet (2-H) at δ 4.93, coupled to both 1-H and 3-H and a doublet at δ 4.52 (3-H). The regioselectivity of iodolactonisation of **10** to **16** is striking since there are three possible products (see Scheme 3). Indeed, Corey and Danheiser[11] have reported the bromo lactonisation of the bicyclic dienoic acid **12** to a mixture of bromo lactones *via* routes *a* and *b*. Other dienophiles that have been examined in this system are $H^+(CF_3CO_2H)$ which proceeds[12] by route *a* and *m*-chloroperbenzoic acid (MCPBA) which gives[9] the isoGA$_3$ structure **7** *via* route *c*.



Scheme 3

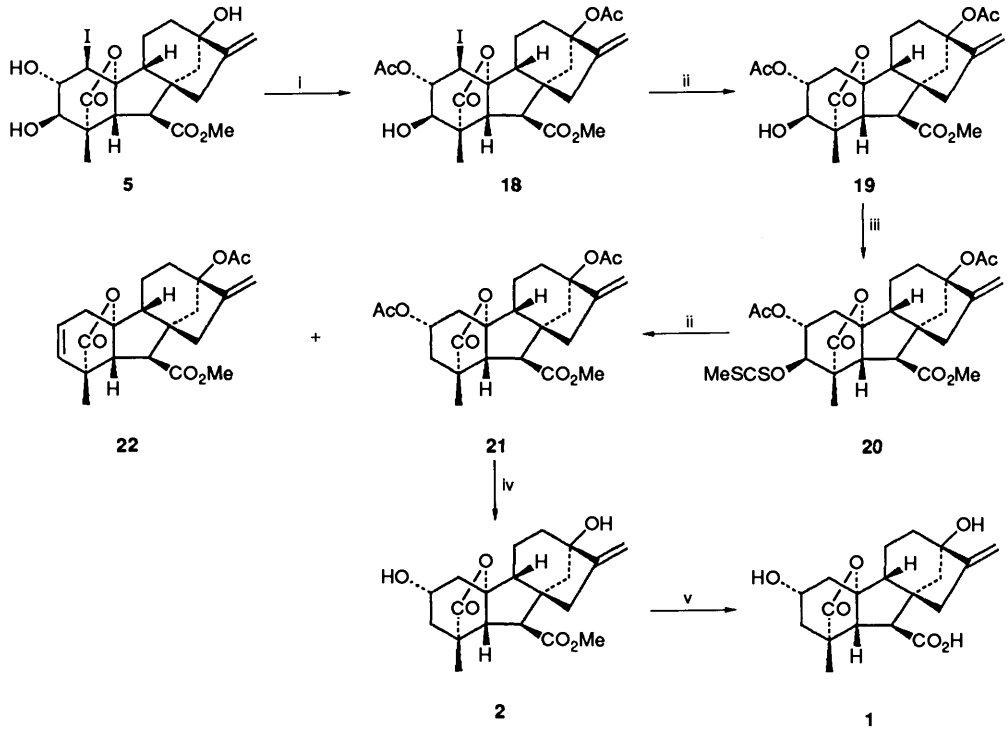
Reduction of the iodo lactone **16** with tributylstannane gave 3-deoxy-isoGA$_3$ methyl ester **17** in 98% yield. The synthesis of GA_{81} **1** was then completed as originally envisaged by hydrolysis–iodo lactonisation (*cf.* Scheme 1) to **6** then reductive deiodination to GA_{81} methyl ester **2**. The overall yield from GA_3 was 18%.

Route 2 (*Scheme* 4).—The key step in this route from GA_3 **4** to GA_{81} **1** was the selective protection of the 2α- and 13-hydroxy groups in the iodo lactone **5** to permit deoxygenation at C-3 *via* the xanthate **20**. The iodo lactone **5** was prepared from GA_3 in 69% yield using the one-pot sequence, outlined in Scheme 1, followed by methylation.

Selective protection of the 2α- and 13-hydroxy groups was achieved with acetic anhydride in the presence of toluene-*p*-sulphonic acid. The selectivity of this reaction arises from the transannular interaction of the 1β-iodide with the 3β-alcohol which sterically hinders the formation of the 3β-acetate. Reduction of the iodide **18** with tributylstannane gave the 2α,13-diacetate **19**. The ^1H NMR spectrum of **19** displayed singlets at δ 2.03 and 2.05, assigned to the two acetoxy groups, a broad singlet at δ 3.75 assigned to 3α-H and a multiplet at δ 4.97 attributed to the equatorial 2β-H.

Reaction of the diacetoxy alcohol **19** with sodium hydride, carbon disulphide and methyl iodide returned the xanthate **20** which was immediately reduced with tributylstannane to the 2α,13-diacetate **21** in 65% yield from **19**. A competing reaction was the *trans*-diaxial elimination of the 2α-acetate and 3β-dithiocarbonate to give GA_5-13-acetate **22**. At 80 °C **22** was formed as a by-product (*ca.* 10%). However when the reaction mixture was heated to reflux in toluene **22** was the major product (55%).

Finally, deprotection of 2-*epi*-GA_{29}-2,13-diacetate 7-methyl



Scheme 4 *Reagents:* i, Ac_2O, TsOH; ii, Bu_3SnH, AIBN (azoisobutyronitrile); iii, NaH, CS_2, MeI; iv, aq. K_2CO_3, MeOH; v, PrSNa, HMPA (hexamethylphosphoramide)

ester **21**, first with aqueous potassium carbonate in methanol to give 2-*epi*-GA_{29} methyl ester **2** and then with sodium propanethiolate in hexamethylphosphoramide (HMPA) gave GA_{81} **1** identical (GLC–MS) with the natural product. The overall yield of GA_{81} methyl ester **2** by this route was 21%.

Since the 2α-hydroxy group of a C_{19}-gibberellin may be efficiently inverted to the 2β-orientation,[13] these syntheses of 2-*epi*-GA_{29} **1** provide an alternative route for the preparation of GA_{29} **3**.

Experimental

General experimental details have been described in a previous paper.[15] *J* values are given in Hz.

ent-1α-*Bromo*-10β,13-*dihydroxy*-20-*norgibberella*-2,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* **14** *and* ent-3β-*Bromo*-10β,13-*dihydroxy*-20-*norgibberella*-1,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* **15**.—To gibberellin A_3 methyl ester **13** (950 mg) in acetone (20 cm^3) with pyridine (2 cm^3) was added resublimed carbon tetrabromide (550 mg) and triphenylphosphine (1.7 g). The solution was heated to reflux for 5 h and then evaporated under reduced pressure using toluene to remove the pyridine azeotropically. The resultant gum (2.0 g) was fractionated by flash chromatography (15 × 5 cm) eluted with the following mixtures of ethyl acetate in light petroleum: 20% (200 cm^3), 30% (200 cm^3), 40% (200 cm^3) and 45% (200 cm^3). Forty fractions of 20 cm^3 were collected. Fractions 20–26 contained the 1β-*bromide* **14** (748 mg) $\delta_H(CDCl_3)$ 1.26 (s, 18-H_3), 2.64 (d, *J* 10, 6-H), 3.20 (d, *J* 10, 5-H), 3.75 (s, OCH_3), 4.69 (dd, *J* 3.5, 1, 1-H), 5.00 and 5.27 (both br s, 17-H_2), 5.73 (d, *J* 9, 3-H) and 6.02 (dd, *J* 9, 3.5, 2-H); *m/z* 424 [(M^+ + 2) 6%], 422 (M^+, 6%), 390 (3), 363 (10), 343 (M^+ − Br, 23%), 310 (14), 298 (17), 283 (11), 255 (11), 239 (100) and 221 (25).

Fractions 28–38 yielded the 3α-*bromide* **15** (185 mg), $\delta_H(CDCl_3)$ 1.22 (s, 18-H_3), 2.71 (d, *J* 10.5, 6-H), 3.07 (d, *J* 10.5, 5-H), 3.74 (s, OCH_3), 4.82 (dd, *J* 2.5, 1.5, 3-H), 4.97 and 5.29 (each br s, 17-H_2) 5.75 (dd, *J* 9, 1.5, 1-H) and 5.86 (dd, *J* 9, 2.5, 2-H); *m/z* 424 [(M^+ + 2) 13%], 422 (M^+, 13), 390 (10), 343 (60), 277 (38) and 239 (100).

ent-13-*Hydroxy*-20-*norgibberella*-1(10),2,16-*triene*-7,19-*dioic Acid* 7-*Methyl Ester* **10**.—A mixture of the 1β-bromide **14** (640 mg) and 3α-bromide **15** (205 mg) in ethyl acetate (100 cm^3) and acetic acid (10 cm^3) was stirred with activated zinc (8 gm) for 1 h at room temperature. After filtration, the solvent was removed under reduced pressure to leave a gum which was flash chromatographed (15 × 5 cm) using ethyl acetate–light petroleum–acetic acid (50:50:1 then 55:45:1 then 60:40:1) to give the *title compound* **10** (639 mg) (Found: M^+, 344.161. $C_{20}H_{24}O_5$ requires *M*, 344.162) λ_{max}(EtOH)/nm 270 (5200); $\delta_H(CDCl_3)$ 1.33 (s, 18-H_3), 3.08 (d, *J* 4, 6-H), 3.3 (br s, 5-H), 3.70 (s, OMe), 4.94 and 5.08 (each br s, 17-H_2), 5.41 (d, *J* 10, 3-H), 5.62 (dt, *J* 5, 2.5, 1-H) and 6.10 (dd, *J* 10, 5, 2-H); $\delta_C(C_5D_5N)$ 19.26 (C-11), 26.64 (C-18), 38.82 and 39.37 (C-12 and C-14), 46.70, 50.33 and 53.41 (C-5, C-6, C-9), 49.72 (C-15), 51.61 (OCH_3), 52.62 (C-8), 60.25 (C-4), 78.71 (C-13), 106.09 (C-17), 112.04 (C-1), 125.47 and 129.62 (C-2 and C-3), 146.04 (C-10), 156.26 (C-16), 176.13 and 176.68 (C-7 and C-19).

Cyclic Dithiocarbonate **9**.—A solution of isogibberellin A_3 methyl ester **7** (500 mg) and 18-crown-6 (10 mg) in dry tetrahydrofuran (THF) (10 cm^3) was added, under N_2, to a suspension of potassium hydride (35% oil dispersion, washed with light petroleum; 350 mg) in THF. Carbon disulphide (1 cm^3) was added and the mixture stirred overnight. Ethanol (5 cm^3) was added dropwise to destroy residual potassium hydride and then the mixture was added to water (30 cm^3) which was acidified to pH 3 with dilute hydrochloric acid and extracted with ethyl acetate. Flash chromatography of the recovered gum, using ethyl acetate–light petroleum–acetic acid (80:20:1 then 85:15:1, 90:10:1 and 100:0:1; 100 cm^3 each collected in 25 fractions) gave in fractions 6–9 the 1(10),2,16-*trienoic acid* **10** (101 mg) described above. Fractions 15–21

contained the cyclic xanthate **10** (275 mg) as a yellow gum; $\delta_H(CDCl_3)$ 1.56 (s, 18-H_3), 3.21 (s, 5-H and 6-H), 3.75 (s, OMe), 4.96 (br s, 2-H), 5.01 and 5.10 (each br s, 17-H_2) 5.20 (d, *J* 5.5, 3-H) and 5.34 (br s, 1-H); $\delta_C(CDCl_3)$ 18.39 (C-11), 22.42 (C-18), 36.85 (C-12 and C-14), 40.87, 44.90, 46.40, 50.36 (C-9, C-5, C-6 and C-2), 48.15 (C-8 and C-15), 49.39 (C-4), 52.12 (OCH_3), 79.74 (C-13), 91.50 (C-3), 107.29 (C-17), 113.07 (C-1), 142.97 (C-10), 151.87 (C-16), 175.01 and 175.20 (C-7 and C-19), 210.75 (C=S). Fractions 10–14 contained a mixture (96 mg) of **9** and **10**.

Reduction of the Cyclic Xanthate **9** *with Tributylstannane.*—The cyclic xanthate **9** (275 mg) and the mixed fractions above (96 mg) were heated to reflux in toluene with tributylstannane (540 mg) and 2,2′-dimethyl-2,2′-azo(propiononitrile) (5 mg). After 2 h the solvent was removed under reduced pressure and the resultant liquid applied to a flash chromatography column (15 × 5.5 cm). The column was eluted with mixtures of ethyl acetate–light petroleum–acetic acid as follows. Initially 200 cm^3 of 20:80:1 was used to remove the organo-tin residues. Then 100 cm^3 portions of 45:55:1, 50:50:1, 55:45:1 and 70:30:1 were passed through the column and collected in 30 fractions of *ca.* 13 cm^3 each. Fractions 6–9 contained the 1(10),2,16-triene acid **10** (232 mg) described above. Fractions 15–18 gave the *isomeric* 1,9,16-*trienoic acid* **11** (63 mg), λ_{max}(EtOH)/nm 247 (3590) (Found: M^+, 344.161. $C_{20}H_{24}O_5$ requires *M*, 344.162); $\delta_H(CDCl_3)$ 1.26 (s, 18-H_3), 3.33 (m, 5-H), 3.51 (d, *J* 8, 6-H), 3.73 (s, OCH_3), 4.97 and 5.15 (both br s, 17-H_2) 5.72 (m, 2-H) and 6.28 (d, *J* 5, 1-H); $\delta_C(CDCl_3)$ 106.06 (C-17), 122.11 and 127.45 (C-1 and C-2), 127.46 and 136.70 (C-9 and C-10), 153.79 (C-16), 175.12 and 182.05 (C-7 and C-19); *m/z* 344 (M^+, 100%), 326 (25), 316 (10), 312 (66), 298 (20), 294 (42), 284 (43) and 239 (97).

ent-2β,13-*Dihydroxy*-3α-*iodo*-20-*norgibberella*-1(10),16-*diene*-7,19-*dioic Acid* 19,2-*Lactone* 7-*Methyl Ester* **16**.—The 1(10),2,16-triene acid **10** (40 mg) in THF (4 cm^3), dichloromethane (4 cm^3) and saturated aqueous sodium hydrogen carbonate (9 cm^3) was vigorously stirred with iodine (48 mg) at 20 °C for 1 h. The organic phase was then separated and washed with aqueous sodium thiosulphate and then water. After evaporation, the product was purified by flash chromatography (15 × 2 cm) with ethyl acetate–light petroleum (1:1, 50 cm^3) and ethyl acetate–light petroleum (3:2, 100 cm^3), collected in 20 fractions. Removal of solvent from fractions 6–9 gave the *title compound* **16** (38 mg) as a foam [Found: (M^+ − 127) 343.155, $C_{20}H_{23}O_5$ (*M* − 127) requires 343.155]; $\delta_H(CDCl_3)$ 1.16 (s, 18-H_3), 2.58 (d, *J* 7, 6-H), 3.26 (dd, *J* 7, 2.5, 5-H), 3.75 (s, OCH_3), 4.52 (d, *J* 5, 3-H), 4.93 (t, *J* 5, 2-H), 4.99 and 5.14 (both br s, 17-H_2) and 5.82 (dd, *J* 5, 2.5, 1-H); *m/z* 470 (M^+, 0.5%), 343 (7), 311 (20), 298 (22), 283 (38), 269 (18), 239 (100), 221 (28) and 209 (18).

On a larger scale the triene acid **10** (500 mg) gave the iodo lactone **16** (620 mg) in 91% isolated yield.

ent-2β,13-*Dihydroxy*-20-*norgibberella*-1(10),16-diene-7,19-*dioic Acid* 19,2-*Lactone* 7-*Methyl Ester* **17**.—The 3β-iodo lactone **16** (500 mg) in toluene (20 cm^3) was heated to reflux with tributylstannane (600 mm^3) and 2,2′-dimethyl-2,2′-azo-(propiononitrile) (3 mg) for 1 h. After removal of the solvent, flash chromatography was carried out as follows on a 15 × 2.5 cm column. The loaded column was first eluted with 20% ethyl acetate in light petroleum to remove the organo-tin residues. Subsequent elution was with 50% ethyl acetate (50 cm^3), 60% ethyl acetate (50 cm^3) and 70% ethyl acetate (100 cm^3) with the collection of 15 fractions. The required *lactone* **17** (360 mg) was recovered from fractions 4–8 (Found: M^+, 344.162. $C_{20}H_{24}O_5$ requires *M*, 344.162); $\delta_H(CDCl_3)$ 1.25 (s, 18-H_3), 2.59 (d, *J* 6, 6-H), 3.18 (dd, *J* 6, 2.5, 5-H), 3.74 (s, OCH_3), 4.86 (t, *J* 5, 2-H), 4.97 and 5.13 (each br s, 17-H_2) and 5.95 (dt, *J* 5, 2.5, 1-H).

ent-2β,10β,13-*Trihydroxy*-1α-*iodo*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* **6**.—The 19,2-lactone **17** (410 mg) in THF (25 cm^3) was stirred with 0.5 mol dm^{-3} aqueous potassium hydroxide (25 cm^3) at room temp. for 48 h and then at reflux for 2 h. After cooling the pH was adjusted to pH 9 with hydrochloric acid. Iodine (450 mg) and dichloromethane (50 cm^3) were added and the reaction mixture stirred vigorously for 2 h at room temperature. The organic layer was recovered and washed with aqueous sodium thiosulphate and then water. The product obtained by evaporation under reduced pressure was purified by flash chromatography on a 15 × 2.5 cm column packed with silica and eluted with 45% ethyl acetate in light petroleum (100 cm^3), 50% ethyl acetate (100 cm^3) and 60% ethyl acetate (100 cm^3). Fifteen fractions were collected and evaporation of 8–14 gave the 1β-*iodo lactone* **6** (210 mg) (Found: M^+, 488.068, $C_{20}H_{25}IO_6$ requires *M*, 488.068); $\delta_H(CDCl_3)$ 1.11 (s, 18-H_3) 2.66 (d, *J* 10, 6-H), 3.37 (d, *J* 10, 5-H), 3.75 (s, OCH_3), 4.49 (s, 1-H), 4.61 (d, *J* 4, 2-H) and 4.99 and 5.27 (each, br s, 17-H_2); *m/z* 488 (M^+, 20%), 438 (14), 429 (42), 361 (34), 343 (19), 329 (18), 315 (32), 301 (52), 283 (46), 268 (33) and 255 (100).

ent-2β,10β,13-*Trihydroxy*-20-*norgibberell*-16-*ene*-17,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* (*Gibberellin* A_{81} *Methyl Ester*) **2**.—A suspension of the 1β-iodo lactone **6** (180 mg) in toluene (45 cm^3) was heated to reflux with tributylstannane (200 mm^3) and 2,2′-dimethyl-2,2′-azo(propiononitrile) (3 mg) for 1.5 h. Removal of the toluene under reduced pressure gave an oil which was loaded onto a flash chromatography column (15 × 2.5 cm). The column was eluted initially with 20% ethyl acetate in light petroleum to remove tributyltin compounds. Further elution was with 60% ethyl acetate (100 cm^3), 75% ethyl acetate (100 cm^3) and 85% ethyl acetate (100 cm^3) collected in 20 fractions. Fractions 8–15 gave *gibberellin* A_{81} *methyl ester* **2** (130 mg) as a gum (Found: M^+, 362.173, $C_{20}H_{26}O_6$ requires *M*, 362.173); $\delta_H(CDCl_3)$ 1.10 (s, 18-H_3), 2.60 (d, *J* 10, 5-H), 2.73 (d, *J* 10, 6-H), 3.72 (s, OCH_3), 4.30 (t, *J* 4, 2-H) and 4.95 and 5.25 (each br s, 17-H_2); *m/z* 362 (M^+, 32%), 344 (14), 330 (19), 316 (15), 312 (100), 303 (61), 284 (32) and 231 (22).

ent-2β,3α,10β,13-*Tetrahydroxy*-1α-*iodo*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* **5**.—Gibberellin A_3 **4** (1 g) in THF (10 cm^3) and aqueous potassium hydroxide (0.8 mol dm^{-3}, 10 cm^3) was stirred for 15 h at room temperature. The solution was adjusted to pH 9 with 2 mol dm^{-3} hydrochloric acid. Methylene dichloride (20 cm^3) and iodine (750 mg) were added and stirred vigorously for 2 h at room temperature. The organic layer was decanted off. The aqueous layer was acidified to pH 2 with 2 mol dm^{-3} hydrochloric acid and extracted with ethyl acetate. The extract was washed with aqueous sodium thiosulphate and then with water, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was taken up in methanol (10 cm^3) and treated with ethereal diazomethane at 0 °C. The solvent was removed under reduced pressure and the product purified by flash chromatography. Elution with 80% ethyl acetate in light petroleum gave 1β-iodoGA_{56} methyl ester **5** which was crystallised from ethyl acetate–light petroleum (828 mg), m.p. 122–123 °C (lit.,[14] m.p. 118–120 °C) (Found: M^+, 504.066. Calc. for $C_{20}H_{25}IO_7$, *M*, 504.067) $\delta_H(CD_3)_2CO$ 1.13 (s, 18-H_3), 2.63 (d, *J* 11, 6-H), 3.73 (s, OCH_3), 3.77 (br s, 3-H), 3.85 (d, *J* 11, 5-H), 4.43 (br s, 2-H), 4.64 (br s, 1-H), 4.92 and 5.21 (2 br s, 17-H_2); *m/z* 504 (M^+, 11%), 445 (15), 442 (10), 297 (66), 254 (100), 195 (8) and 128 (41).

119ent-2β,13-*Diacetoxy*-3α,10β-*dihydroxy*-1α-*iodo*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* **18**.—1β-Iodogibberellin A_{56} methyl ester **5** (0.5 g), acetic anhydride (15 mm^3) and toluene-*p*-sulphonic acid (5 mg) were stirred in acetone (15 cm^3) for 1 h at room temp. Work-up gave the crude product which was purified by flash chromatography.

Elution with 45% ethyl acetate in light petroleum gave 1β-*iodo*GA_{56} 2,3-*diacetate* 7-*methyl ester* **18** as a gum (0.42 g) (Found: M^+, 588.0870. $C_{24}H_{29}O_9I$ requires *M*, 588.0858); δ_H 1.20 (s, 18-H_3), 2.03 and 2.06 (2 s, 2 × $OCOCH_3$), 2.72 (d, *J* 10, 6-H), 3.75 (s, OCH_3 masking 3-H), 3.83 (d, *J* 10, 5-H), 4.28 (br s, 1-H), 5.03 and 5.16 (2 br s, 17-H_2) and 5.46 (2 br s, 2-H); *m*/*z* 588 (M^+, 8%), 546 (10), 444 (4), 402 (3), 384 (5), 352 (6), 341 (6), 339 (9), 299 (5), 298 (5), 297 (13), 221 (8), 91 (7) and 43 (100).

ent-2β-13-*Diacetoxy*-3α,10β-*dihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* **19**.—1β-Iodogibberellin A_{56} 2,13-diacetate 7-methyl ester **18** (0.42 g) in toluene (50 cm^3) was heated to reflux with 2,2′-dimethyl-2,2′-azo(propiononitrile) (10 mg) and tributylstannane (100 mm^3) was added. The mixture was heated to reflux for 1.5 h and the solvent was then removed under reduced pressure. Purification by flash chromatography eluting with 70% ethyl acetate in light petroleum gave GA_{56} 2,13-*diacetate* 7-*methyl ester* **19** as a gum (310 mg) (Found: M^+, 462.1904. $C_{24}H_{30}O_9$ requires *M*, 462.1889); δ_H 1.16 (s, 18-H_3), 2.03 and 2.05 (2 s, 2 × $OCOCH_3$), 2.75 (d, *J* 11, 6-H), 3.28 (d, *J* 11, 5-H), 3.68 (br s, OH), 3.73 (s, OCH_3), 3.75 (br s, 3-H), 4.97 (m, 17-H and 2-H) and 5.16 (br s, 17-H); *m*/*z* 462 (M^+, 45%), 444 (13), 420 (70), 402 (19), 221 (20), 91 (12) and 43 (100).

ent-2β,13-*Diacetoxy*-10β-*hydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* **21**.—Sodium hydride (60% dispersion in oil; 400 mg) was washed with light petroleum and then THF (5 cm^3) was added. GA_{56} 2,3-diacetate 7-methyl ester **19** (300 mg) in THF (2 cm^3), carbon disulphide (400 mm^3) and 18-crown-6 ether (10 mg) were added. The reaction mixture was stirred for 6 h at room temp. under nitrogen. Methyl iodide (400 mm^3) was added and the mixture stirred for a further 2 h at room temp. Work-up gave the crude dithiocarbonate **20** δ_H 1.13 (s, 18-H_3), 2.03 and 2.07 (2 s, 2 × $OCOCH_3$), 2.62 (s, OCS_2CH_3), 2.75 (d, *J* 10.5, 6-H), 3.27 (d, *J* 10.5, 5-H), 3.75 (s, OCH_3), 5.00 (br s, 17-H), 5.16 (m, 2-H and 17-H) and 5.76 (s, 3-H).

The crude dithiocarbonate **20** in toluene (60 cm^3) was heated to 80 °C with tributylstannane (150 mm^3) and 2,2′-dimethyl-2,2′-azo(propiononitrile) (10 mg) for 1 h. Further tributylstannane (150 mm^3) and 2,2′-dimethyl-2,2′-azo(propiononitrile) (10 mg) were added and the reaction mixture heated to 80 °C for 1 h. The solvent was removed under reduced pressure and the mixture purified by flash chromatography. Elution with 35% ethyl acetate in light petroleum gave GA_5 13-acetate 7-methyl ester **22** as a gum (22 mg), δ_H 1.25 (s, 18-H_3) 2.02 (s, $OCOCH_3$), 2.65 (d, *J* 10, 5-H), 2.81 (d, *J* 10, 6-H), 3.73 (s, OCH_3), 4.98 and 5.14 (2 br s, 17-H_2), 5.67 (br d, *J* 9, 3-H) and 5.81 (dt, *J* 9 and 3, 2-H); *m*/*z* 446 (M^+, 47%), 415 (15), 405 (24), 404 (91), 386 (37), 344 (33), 312 (46), 284 (31), 282 (46) and 43 (100). Further elution with 50% ethyl acetate in light petroleum gave 2-*epi*-GA_{29} 2,13-diacetate 7-methyl ester **21** which crystallised from ethyl acetate–light petroleum (193 mg), m.p. 162–165 °C (lit.,[5] m.p. 167–168 °C) (Found: M^+, 446.1970. Calc. for $C_{24}H_{30}O_8$, *M*, 446.1940); δ_H 1.09 (s, 18-H_3), 2.02 and 2.03 (2 s, 2 × $OCOCH_3$), 2.64 (d, *J* 10, 5-H), 2.75 (d, *J* 10, 6-H), 3.73 (OCH_3), 4.98 and 5.14 (2 br s, 17-H_2) and 5.22 (m, 2-H); *m*/*z* 446 (M^+, 40%), 415 (12), 404 (85), 386 (29), 344 (32), 312 (41), 282 (49), 155 (16), 91 (19) and 43 (100).

ent-2β,10β,13-*Trihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* (*Gibberellin* A_{81} *Methyl Ester*) **2**.—2-*epi*-Gibberellin A_{29} 2,13-diacetate 7-methyl ester **21** (80 mg) in methanol (4 cm^3) and aqueous potassium carbonate (1 cm^3) was stirred for 24 h at room temp. Work-up gave a single product by TLC which was purified by flash chromatography. Elution with 85% ethyl acetate–light petroleum gave gibberellin A_{81} methyl ester **2** which crystallised from acetone–light petroleum as needles (55 mg), m.p. 182–183 °C (lit.,[5] m.p. 181–183 °C), δ_H 1.10 (s, 18-H_3), 2.61 (d, *J* 10, 5-H), 2.73 (d, *J* 10, 6-H), 3.73 (s, OCH_3), 4.30 (m, 2-H), 4.95 and 5.25 (2 br s, 17-H_2); *m*/*z* 362 (M^+, 66%), 344 (24), 312 (100), 303 (59), 284 (42), 239 (27), 135 (34) and 91 (36).

ent-2β,10β,13-*Trihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* (*Gibberellin* A_{81}) **1**.—Sodium hydride (60% dispersion in oil; 240 mg) was washed with light petroleum. Freshly distilled hexamethylphosphoramide (HMPA) (5 cm^3) was added *via* a syringe under nitrogen. The mixture was cooled to 0 °C and propanethiol (0.7 cm^3) was added dropwise with stirring. The reagent was stirred for 1 h at room temp. and then allowed to settle.

A portion (2 cm^3) of the supernatant sodium propanethiolate–HMPA solution was added to *epi*-GA_{29} 7-methyl ester **2** (30 mg) and the mixture stirred for 4 h at room temp. Work-up gave a gum which on purification by flash chromatography eluting with ethyl acetate–light petroleum–acetic acid (80:19:1) gave *gibberellin* A_{81} **1** (8 mg) as a gum; $\delta_H[(CD_3)_2CO]$ 1.04 (s, 18-H_3), 2.72 (br s, 5-H and 6-H), 4.25 (m, 2-H), 4.84 and 5.18 (2 br s, 17-H_2); *m*/*z* (Me/TMS) 506 (M^+, 100%), 459 (11), 389 (11), 375 (26), 303 (22), 291 (11), 235 (8), 207 (27) and 167 (14).

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