Partial Synthesis of 20-Norgibberellin A_{12} and Structural Elucidation of a Metabolite Detected in Oilseed Rape, *Brassica napus*

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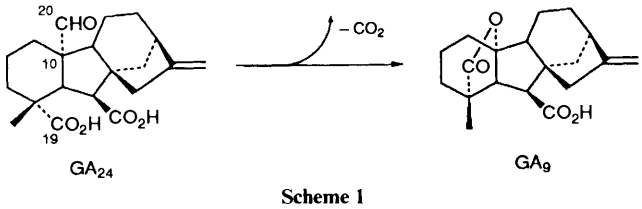
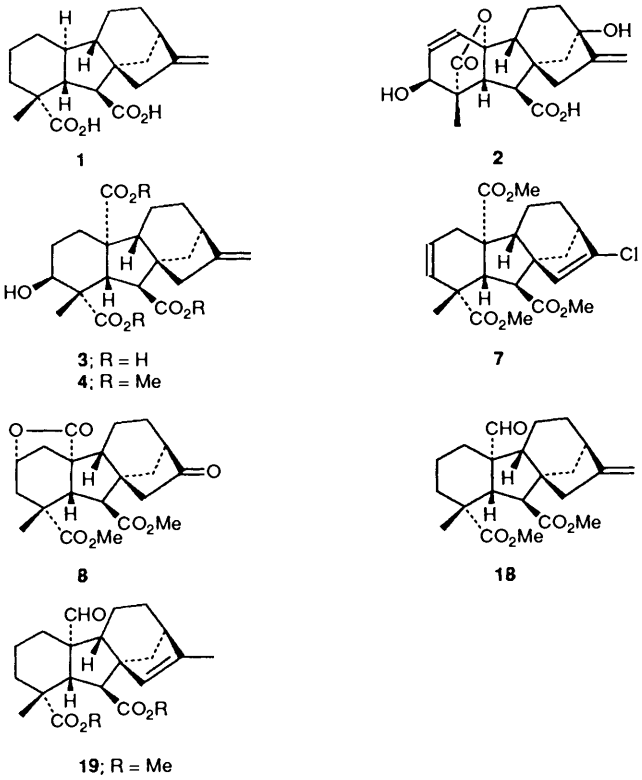
20-Norgibberellin A_{12} was synthesised from gibberellin A_{13} trimethyl ester in 6% overall yield. The structure of a metabolite previously detected by GC–mass spectrometry in a methylated extract from shoots of oilseed rape was elucidated.

Recently Hedden *et al.*[1] detected an unknown metabolite by GC–mass spectrometry in a methylated extract of three week old shoots of spring oilseed rape cv Petranova (*Brassica napus* L. ssp *napus*). They suggested that the compound was a C_{19}-dicarboxylic acid related to gibberellin A_{24}. During gibberellin biosynthesis (Scheme 1) GA_{24} is directly metabolised to GA_9



Scheme 1

with the loss of carbon-20 and concomitant formation of the 19,10γ-lactone.[2] Since the highest ion in the EI spectrum of the unknown is at *m/z* 346, a possible structure is **1** in which carbon-20 has been lost from GA_{24} without formation of the 19,10-lactone. In this paper we describe the synthesis of **1** from gibberellin A_{13} trimethyl ester **4** and show that it is different from the metabolite detected in extracts of oilseed rape. However further investigations led to the successful structural elucidation of the natural product.



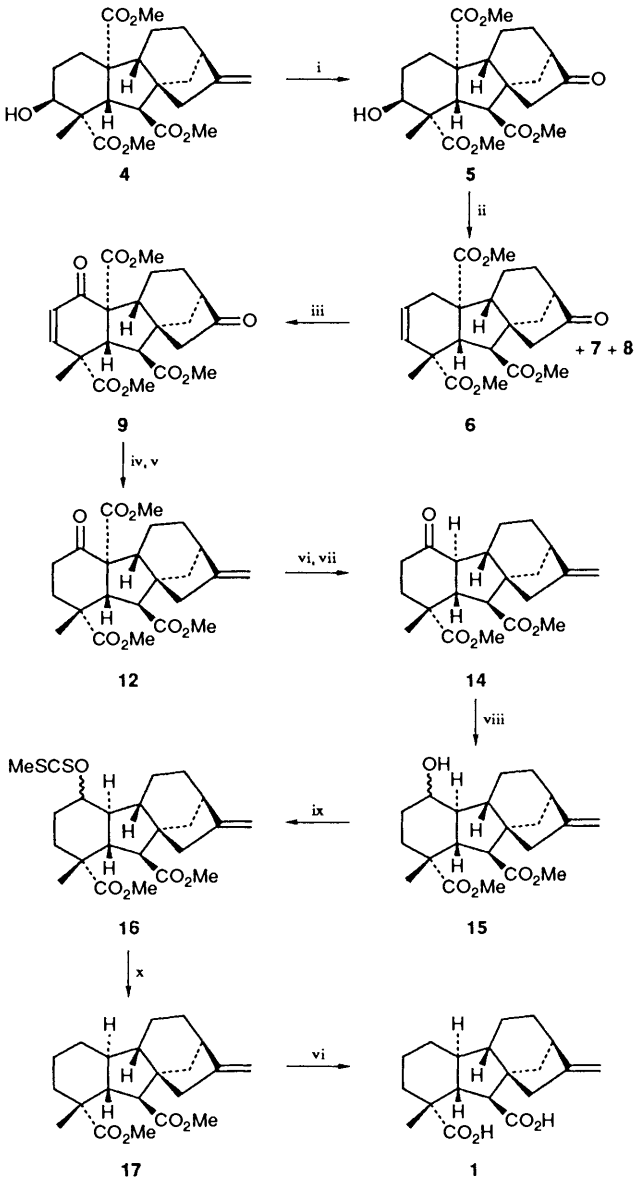
Results and Discussion

The synthetic route to 20-norgibberellin A_{12} **1** from GA_{13} trimethyl ester **4** is shown in Scheme 2. The key step of the pathway involves oxidation at C-1 to give the ketone required to facilitate the selective removal of the 20-carboxylic acid.[3]

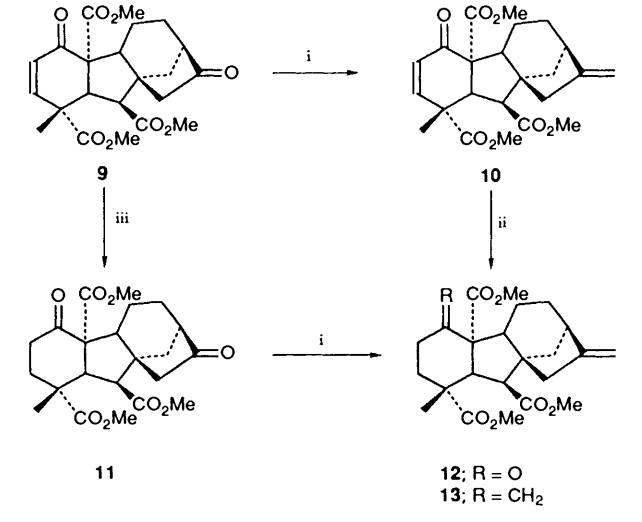
The starting material, GA_{13} trimethyl ester **4**, was obtained by methylation of a commercially available mixture of GA_{13} **2** and GA_3 **3** followed by purification of the mixture by flash chromatography. The exocyclic olefin of **4** was oxidatively cleaved with sodium periodate in the presence of a catalytic amount of osmium tetroxide to give the 17-norketone **5** in 84% yield. Reaction of **5** with phosphorus oxychloride gave, as the major product, the required olefin **6** and minor amounts of the 16-chloro 2,15-diene **7** and a lactone **8**. The ^1H NMR spectrum of the lactone **8** displayed singlets at δ3.70 and 3.73 assigned to the 7- and 19-methyl esters and a triplet at δ4.73 (*J* 5 Hz) attributed to the 2β-proton. The structure of the 20,2-lactone **8** was unambiguously confirmed by X-ray diffraction studies (to be published at a later date). No 20,3-lactone was isolated from the reaction mixture.

The carbonyl function was introduced at C-1 by allylic oxidation of the 2,3-olefin **6** with *tert*-butyl chromate to give the known[3] enone **9** in 52% yield. Removal of carbon-20 was not attempted until the exocyclic double bond was reconstructed. The selective methylenation of the 1,16-dione **9** by the ylide generated from methyltriphenylphosphonium bromide was examined before and after saturation of the 2,3-double bond (Scheme 3). The Wittig reaction on **9** gave a quantitative yield of the required 16,17-olefin **10**. However attempts to reduce selectively the 2,3-double bond of **10** with tributyltin hydride and tetrakistriphenylphosphinepalladium(0),[4,5] gave only a 20% yield of **12**. Hence the alternative route was favoured *i.e.* saturation of the 2,3-olefin of **9** by catalytic hydrogenation followed by methylenation to give the required 1-oxo-GA_{25} trimethyl ester **12** in 66% yield and the minor 1,16-dimethylenation product **13**.

In previous studies,[3] lithium iodide has been used to effect the removal of carbon-20 in the dione **11** by ester hydrolysis and decarboxylation. Reaction of 1-oxo-GA_{25} trimethyl ester **12** under these conditions gave an intractable gum. However, reaction of **12** with sodium propanethiolate in hexamethylphosphoramide[6] provides a mild and effective method for the hydrolysis of the methyl esters and subsequent decarboxylation



Scheme 2 *Reagents:* i, OsO_4, $NaIO_4$; ii, $POCl_3$, pyr.; iii, Bu^tCrO_4; iv, H_2, 10% Pd on $CaCO_3$; v, $Ph_3P^+CH_3Br^-$, NaH; vi, PrSNa, HMPA; vii, CH_2N_2; viii, $NaBH_4$, MeOH; ix, NaH, CS_2, MeI; x, Bu_3SnH, AIBN



Scheme 3 *Reagents:* i, $Ph_3P^+CH_3Br^-$, NaH; ii, $(Ph_3P)_4Pd$, Bu_3SnH; iii, H_2, 10% Pd on $CaCO_3$

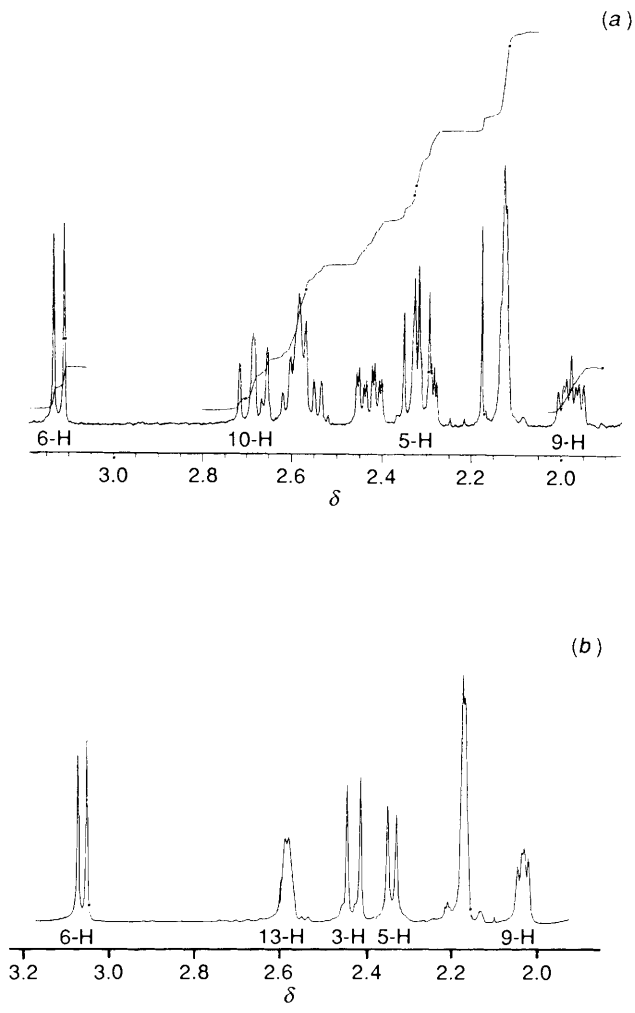


Fig. 1 400 MHz ^1H NMR spectra of (*a*) **14** in $CDCl_3$ and (*b*) [2,2,-10-$^2H_3$]-**14** in $CHCl_3$

at carbon-20 giving, after methylation with ethereal diazomethane, the 1-oxodimethyl ester **14** as the sole product in 84% yield. The stereochemistry of the A/B ring junction in **14** was established by NMR spectroscopy.

Fig. 1 shows the region δ1.9–3.2 of the ^1H NMR spectrum of **14**. From proton decoupling experiments it was apparent that $J_{5,6}$ 9.3 Hz, $J_{5,10}$ 13 Hz and $J_{9,10}$ 12.5 Hz, indicating that the 10-proton is in the α-configuration. The formation of the A/B ring fusion was in accord with previous studies and was confirmed by X-ray crystallography (to be published elsewhere). Treatment of the ketone **14** with sodium methoxide in methanol returned starting material, none of the corresponding 10β-H epimer was detected. Reaction of the ketone **14** with sodium methoxide in methanol–OD gave a single product **14** with an 86% incorporation of three deuterium atoms. The positions of the deuterium atoms were determined by an examination of the ^1H NMR (Fig. 1b) and ^2H NMR spectra and found to be located at 2α,2β and 10α positions (^2H NMR $\delta CHCl_3$: 2.3, 2.58 and 2.7). This result confirms that the enolate at C-10 had indeed been formed during the exchange reaction and the sole product retained the trans A/B ring junction.

The synthesis of 20-nor-GA_{12} **1** was completed by reduction of 1-oxo-20-nor-GA_{12} dimethyl ester **14** with sodium borohydride to give a 1:1.7 mixture of 1α-hydroxy- and 1β-hydroxy-20-nor-GA_{12} dimethyl ester **15** which, without separation, was deoxygenated at C-1 by radical reduction of the corresponding 1-xanthates **16** with tributyltin hydride. Finally hydrolysis of the

methyl esters with sodium propanethiolate in hexamethylphosphoramide gave the required 20-nor-GA_{12} **1** in 6% overall yield from GA_{13} trimethyl ester **4**.

Structural Elucidation of the Metabolite Detected in Oilseed Rape.—A sample of 20-nor-GA_{12} dimethyl ester **17** was compared by GC–mass spectrometry with the unknown metabolite detected in methylated extracts of shoots of oilseed rape. The synthetic sample had a shorter retention time (KRI 2238) than the unknown (KRI 2442) and its fragmentation pattern, although similar to the unknown[7] showed significant differences. Hence the compound in oilseed rape was not 20-nor-GA_{12} **1**.

In order to elucidate the structure of the unidentified metabolite, its mass spectrum was re-examined[7] by chemical ionisation (CI, isobutane). The highest ion in this spectrum was at *m/z* 375 ($M^+ + 1$) consistent with GA_{24} dimethyl ester **18** (MW 374). However the unknown was not GA_{24} dimethyl ester itself (KRI 2485).[7,*] Treatment of GA_{24} dimethyl ester **18** with iodine in benzene under nitrogen led to isomerisation of the 16,17-double bond giving the more stable 15-ene **19**. Comparison of *endo*-GA_{24} dimethyl ester **19** with the unknown by GC–mass spectrometry showed that they were identical. Therefore the metabolite accumulating in oilseed rape was finally assigned the structure *endo*-GA_{24} **20**.

Experimental

General experimental details have been described in a previous paper.[8] *J* Values are given in Hz.

Trimethyl ent-3α-*Hydroxy*-16-*oxo*-17-*norgibberellane*-7,19,20-*trioate* **5**.—Gibberellin A_{13} trimethyl ester **4** (2.92 g) in freshly distilled tetrahydrofuran (THF) (35 cm^3) and water (35 cm^3) was stirred with osmium tetroxide (2 crystals) and sodium periodate (5.0 g) at room temperature for 20 h. The THF was blown off with a stream of nitrogen. The residual aqueous layer was diluted with water (50 cm^3) and then extracted with ethyl acetate (3 × 70 cm^3). The extract was washed with water and dried over anhydrous sodium sulphate. After filtration the solvent was removed under reduced pressure to give a light brown crude product which was purified by flash chromatography. Elution with 80% ethyl acetate in light petroleum afforded the title compound **5** (2.48 g) which crystallised from ethyl acetate–light petroleum as needles, m.p. 188–190 °C (lit.,[3] m.p. 188–190 °C and lit.,[9] m.p. 186–189 °C); δ1.24 (s, 18-H_3), 2.59 (d, *J* 13, 5-H), 3.63, 3.67 and 3.73 (each s, 3 × OCH_3), 3.96 (d, *J* 3, 3-H) and 3.98 (d, *J* 13, 6-H); *m/z* 422 (M^+, 5%), 404 (2), 390 (100), 362 (19), 331 (15), 330 (35), 302 (26), 241 (5), 92 (13) and 59 (29).

Dehydration of the Norketone **5** *with Phosphorus Oxychloride.*—The norketone **5** (2.20 g) in pyridine (10 cm^3) was heated to reflux with phosphorus oxychloride (1.0 cm^3) for 40 min. The cooled mixture was added dropwise to water (70 cm^3), acidified to pH 2 with 2 mol dm^{-3} hydrochloric acid and extracted with ethyl acetate (3 × 60 cm^3). The extracts were combined, washed with water and dried over anhydrous sodium sulfate. After filtration, the solvent was evaporated under reduced pressure to give a gum which was purified by flash chromatography. Elution with 20% ethyl acetate in light petroleum gave trimethyl *ent*-16-chloro-17-norgibberella-2,15-diene-7,19,20-trioate **7** (154 mg) which crystallised from ethyl acetate–light petroleum as needles; m.p. 152–154 °C (lit.,[3] m.p. 150–152 °C); δ1.26 (s, 18-H_3), 2.36 (d, *J* 12, 5-H), 2.92 (dd, *J* 16, 6, 1-H), 3.58, 3.65 and 3.74 (each s, 3 × OCH_3), 3.78 (d, *J* 12, 6-H), 5.54 (dd, *J* 10, 2, 3-H), 5.77 (ddd, *J* 10, 6, 2, 2-H) and 5.81 (br, s, 15-H); *m/z* 422 (M^+, 58%), 390 (66), 363 (33), 362 (23), 330 (100), 302 (32), 243 (72) and 179 (22). The second compound eluted was the required trimethyl *ent*-16-oxo-17-norgibberell-2-ene-7,19,20-trioate **6** (1.36 g) which crystallised from ethyl acetate–light petroleum as needles; m.p. 165–167 °C (lit.,[3] m.p. 165–167 °C); δ1.29 (s, 18-H_3), 2.42 (d, *J* 13, 5-H), 2.96 (dd, *J* 16, 6, 1-H), 3.59, 3.68 and 3.77 (each s, 3 × OCH_3), 3.96 (d, *J* 13, 6-H), 5.57 (dd, *J* 10, 2, 3-H) and 5.78 (ddd, *J* 10, 6, 2, 2-H); *m/z* 404 (M^+, 17%), 372 (35), 345 (25), 344 (13), 313 (53), 312 (96), 285 (73), 284 (16), 225 (100) and 91 (24). Further elution with 80% ethyl acetate in light petroleum gave *ent*-2β-hydroxy-17,19-bis(methoxycarbonyl)-16-oxo-17-norgibberellan-20-oic acid 20,2-lactone **8** (12 mg) which crystallised from ethyl acetate–light petroleum as needles; m.p. 237–239 °C (lit.,[3] m.p. 225–226 °C). δ1.33 (s, 18-H_3), 1.50 (d, *J* 15, 1β-H), 1.70 (d, *J* 12, 3β-H), 2.57 (ddd, *J* 12, 6, 2, 3α-H), 2.47 (d, *J* 12, 5-H), 3.02 (ddd, *J* 15, 5, 2, 1α-H), 3.67 (d, *J* 12, 6-H), 3.70 and 3.73 (each s, 2 × OCH_3) and 4.73 (t, *J* 5, 2-H); *m/z* 390 (M^+, 9%), 359 (25), 358 (100), 330 (12), 299 (10), 270 (6), 227 (9), 193 (6), 128 (4) and 91 (7).

Trimethyl ent-1,16-*Dioxo*-17-*norgibberell*-2-*ene*-7,19,20-*trioate* **9**.—To *tert*-butyl alcohol (60 cm^3) was added chromium trioxide (21.0 g) in portions with stirring at room temperature. The dark brown solution was stirred for a further 20 min and then diluted with carbon tetrachloride (200 cm^3). The aqueous phase was separated off and the organic phase dried over anhydrous sodium sulfate. The drying agent was filtered off and washed with carbon tetrachloride (60 cm^3). The combined filtrates were concentrated to 120 cm^3 under reduced pressure at *ca.* 45 °C.

To a solution of the olefin **6** (428 mg) in refluxing carbon tetrachloride (20 cm^3) was added dropwise a mixture of the above *tert*-butyl chromate–carbon tetrachloride solution (25 cm^3), acetic acid (7 cm^3) and acetic anhydride (3.5 cm^3) over 0.5 h. The mixture was heated under reflux for a further 32 h, cooled to room temperature and then treated with oxalic acid (1.5 g) in water (70 cm^3) for 1.5 h at room temperature with stirring. The organic layer was separated and the aqueous phase was extracted with carbon tetrachloride (2 × 60 cm^3). The combined extracts were washed with water and aqueous sodium hydrogen carbonate and dried. Evaporation under reduced pressure and purification by flash chromatography gave a mixture of the starting material **6** and the enone **9** (114 mg). The second product eluted was the enone **9** (230 mg) which crystallised from ethyl acetate–light petroleum as needles; m.p. 135–137 °C (lit.,[3] m.p. 134–136 °C) (Found: M^+, 418.1637. $C_{22}H_{26}O_8$ requires *M*, 418.1627); δ1.40 (s, 18-H_3), 2.70 (d, *J* 13, 5-H), 3.62, 3.72 and 3.78 (each s, 3 × OCH_3), 4.08 (d, *J* 13, 6-H), 6.10 (d, *J* 10, 2-H) and 6.60 (d, *J* 10, 3-H); *m/z* 418 (M^+, 36%), 386 (100), 358 (35), 327 (17), 326 (16), 299 (44), 239 (26), 225 (26) and 193 (25).

Wittig Reaction on the Enone **9**.—Methyltriphenylphosphonium bromide (4.8 g) was added to a suspension of sodium hydride (1.8 g, 60% in oil; prewashed with light petroleum) in freshly distilled THF (75 cm^3). The mixture was stirred overnight at room temperature under nitrogen. A portion of the above ylide (20 cm^3) was added to the enone **9** (200 mg) under nitrogen at room temperature. The mixture was stirred for 15 min. Acetone (4 cm^3) was added followed by water (6 cm^3). Usual work-up followed by flash chromatography, eluting

* GC–MS results: Unknown metabolite (KRI 2442); *m/z* (EI) 346 (12%), 314 (100), 286 (91), 271 (17), 243 (17), 227 (63), 178 (20) and 105 (8); *m/z* (CI) 375 ($M^+ + 1$, 100%), 343 (45), 314 (11), 286 (7), 199 (5), 125 (9) and 97 (8). GA_{24} dimethyl ester **18** (KRI 2485); *m/z* (EI) 374 (M^+, 12%), 342 (43), 314 (100), 286 (81), 254 (24), 226 (71), 143 (18) and 91 (36); *m/z* (CI) 375 ($M^+ + 1$, 100%), 357 (8), 343 (45), 315 (9), 297 (5), 128 (11) and 83 (19).

with ethyl acetate in light petroleum gave *trimethyl* ent-1-*oxogibberella*-2,16-*diene*-7,19,20-*trioate* **10** (182 mg) which crystallised from ethyl acetate in light petroleum as needles; m.p. 145–147 °C; (Found: M^+, 416.1820. $C_{23}H_{28}O_7$ requires *M*, 416.1835); δ1.25 (s, 18-H_3), 2.72 (d, *J* 13, 5-H), 3.59, 3.71 and 3.76 (each s, 3 × OCH_3), 4.05 (d, *J* 13, 6-H), 4.81 and 4.94 (each br s, 17-H_2), 6.08 (d, *J* 10, 2-H) and 6.58 (d, *J* 10, 3-H); *m/z* 416 (M^+, 15%), 385 (34), 384 (100), 356 (10), 325 (12), 324 (27), 297 (24), 238 (16), 140 (15), 112 (15) and 91 (13).

Attempted Reduction of the Enone **10** *with Tributyltin Hydride and Palladium*(0).—To a solution of the enone **10** (60 mg) and tetrakistriphenylphosphinepalladium(0) (10 mg) in dry THF (4 cm^3) was added tributyltin hydride (100 mm^3) dropwise over 2 h with stirring under nitrogen at room temperature. The mixture was stirred overnight and worked up as usual. Purification of the resultant mixture by flash chromatography gave *trimethyl* ent-1-*oxogibberell*-16-*ene*-7,19,20-*trioate* **12** (12 mg) as a gum (Found: M^+, 418.2013. $C_{23}H_{30}O_7$ requires *M*, 418.1991); δ1.29 (s, 18-H_3), 2.41 (d, *J* 13, 5-H), 3.65, 3.71 and 3.73 (each s, 3 × OCH_3), 3.93 (d, *J* 13, 6-H), 4.79 and 4.92 (each br s, 17-H_2); *m/z* 418 (M^+, 10%), 387 (36), 386 (100), 327 (15), 326 (43), 299 (25), 298 (34), 239 (24) and 91 (10), and the starting material **10** (40 mg).

Trimethyl ent-1,16-*Dioxo*-17-*norgibberellane*-7,19,20-*trioate* **11**.—The enone **9** (400 mg) in ethanol (30 cm^3) was stirred with 10% palladium on calcium carbonate (250 mg) at room temperature in an atmosphere of hydrogen for 40 min. The mixture was diluted with ethyl acetate (30 cm^3) and filtered. The catalyst residue was washed with ethyl acetate (2 × 20 cm^3) and filtered. Evaporation of the combined filtrates under reduced pressure gave the 1,16 dione **11** quantitatively (402 mg) which crystallised from ethyl acetate–light petroleum as needles; m.p. 123–125 °C (Found: M^+, 420.1764. $C_{22}H_{28}O_8$ requires *M*, 420.1784); δ1.27 (s, 18-H_3), 2.39 (d, *J* 13, 5-H), 3.68, 3.73 and 3.75 (each s, 3 × OCH_3) and 4.00 (d, *J* 13, 6-H); *m/z* 420 (M^+, 1%), 389 (37), 388 (100), 360 (37), 301 (28), 300 (15), 241 (10), 142 (46) and 114 (34).

Wittig Reaction of the Dione **11**.—To the dione **11** (390 mg) was added a portion of the ylide solution (28 cm^3, prepared as above) with stirring under nitrogen. The mixture was stirred for 20 min, followed by addition of acetone (4 cm^3) then water (6 cm^3). More water (30 cm^3) was added and the mixture was extracted with ethyl acetate (3 × 50 cm^3). The extracts were dried, evaporated and purified by chromatography. Elution with 5% ethyl acetate in light petroleum afforded *trimethyl* ent-1-*methylenegibberell*-16-*ene*-7,19,20-*trioate* **13** (32 mg) as a gum (Found: M^+, 416.2213. $C_{24}H_{32}O_6$ requires *M*, 416.2199); δ1.14 (s, 18-H_3), 2.23 (d, *J* 13, 5-H), 2.59, 3.67 and 3.71 (each s, 3 × OCH_3), 3.96 (d, *J* 13, 6-H), 4.74, 4.82, 4.86 and 4.91 (each br s, 1-CH_2 and 17-CH_2); *m/z* 416 (M^+, 3%), 384 (20), 372 (24), 356 (20), 324 (100), 312 (49), 296 (66), 284 (63), 237 (68) and 91 (23). Further elution with 20% ethyl acetate in light petroleum gave *trimethyl* ent-1-*oxo*-*gibberell*-16-*ene*-7,19,20-*trioate* **12** (256 mg) also as a gum (Found: M^+, 418.2013. $C_{23}H_{30}O_7$ requires *M*, 418.1991); δ1.29 (s, 18-H_3), 2.41 (d, *J* 13, 5-H), 3.65, 3.71 and 3.73 (each s, 3 × OCH_3), 3.93 (d, *J* 13, 6-H), 4.79 and 4.92 (each br s, 17-H_2); *m/z* 418 (M^+, 10%), 387 (36), 386 (100), 327 (15), 326 (43), 299 (25), 298 (34), 239 (24) and 91 (10).

Dimethyl ent-1-*Oxo*-20-*norgibberell*-16-*ene*-7,19-*dioate* **14**.—To a suspension of sodium hydride (240 mg, 60% in oil, prewashed with light petroleum) in dry hexamethylphosphoramide (5 cm^3) was added propanethiol (0.7 cm^3) with stirring under nitrogen at room temperature. The mixture was stirred for a further 2 h then allowed to stand for 1 h before use.

Compound **12** (240 mg) was stirred with a portion of the above propanethiolate–hexamethylphosphoramide solution (4.0 cm^3) overnight under nitrogen at room temperature. After addition of water (25 cm^3), the resultant mixture was acidified to pH 2 with 2 mol dm^{-3} hydrochloric acid and extracted with ethyl acetate (3 × 50 cm^3). The extract was partitioned with saturated aqueous sodium hydrogen carbonate (3 × 30 cm^3). The combined aqueous phase was acidified to pH 2 and extracted with ethyl acetate (3 × 50 cm^3). Chromatography of the resultant gum by elution with ethyl acetate in light petroleum (containing 5% acetic acid) afforded, sequentially the monomethyl esters of ent-1-*oxo*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* (8 mg) as a gum (Found: M^+, 346.1762. $C_{20}H_{26}O_5$ requires *M*, 346.1780); δ1.27 (s, 18-H_3), 3.19 (d, *J* 10, 6-H), 3.70 (s, OCH_3), 4.87 and 4.91 (each br s, 17-H_2); *m/z* 346 (M^+, 23%), 314 (46), 300 (18), 287 (31), 286 (100), 242 (10), 241 (22), 240 (11), 200 (23), 145 (42) and 68 (73) and ent-1-*oxo*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* also as a gum (161 mg). After methylation with ethereal diazomethane, both fractions gave the *keto ester* **14** as a gum (Found: M^+, 360.1921. $C_{21}H_{28}O_5$ requires *M*, 360.1936); δ1.19 (s, 18-H_3), 3.12 (d, *J* 10, 6-H), 3.68 and 3.77 (each s, 2 × OCH_3), 4.87 and 4.90 (each br s, 17-H_2); *m/z* 360 (M^+, 13%), 328 (50), 301 (28), 300 (100), 282 (34), 241 (31), 240 (17), 223 (22), 222 (26) and 91 (14).

Dimethyl ent-1ξ-*Hydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioate* **15**.—To a solution of the keto ester **14** (123 mg) in methanol (25 cm^3) was added sodium borohydride (63 mg) portionwise with stirring at room temperature. After 2.5 h, water (25 cm^3) was added and the resultant mixture was brought to pH 2 with 2 mol dm^{-3} hydrochloric acid and extracted with ethyl acetate (3 × 40 cm^3). Evaporation of the solvent and purification of the resultant gum by flash chromatography gave the 1-*hydroxy compound* **15** as a gum (109 mg) which was a mixture of 1α- and 1β-isomers in a ratio of 1:1.7 (by NMR spectroscopy) (Found: $M^+ - 32$, 330.1839. $C_{21}H_{30}O_5$ requires $M - 32$, 330.1831); *m/z* 362 (M^+, 1%), 344 (1), 330 (17), 312 (18), 285 (30), 284 (100), 242 (6), 241 (4) and 91 (13). 1α-isomer δ1.09 (s, 18-H_3), 3.11 (d, *J* 9, 6-H), 3.54 (m, 1-H), 3.67 and 3.69 (each s, 2 × OCH_3), 4.86 and 4.89 (each br s, 17-H_2); 1β-isomer δ1.12 (s, 18-H_3), 3.02 (d, *J* 9, 6-H), 3.67 and 3.68 (each s, 2 × OCH_3), 4.08 (d, *J* 2, 1-H) and 4.88 (br s, 17-H_2).

Dimethyl ent-1ξ-*Hydroxy*-1-*methylthio*(*thiocarbonyl*)*oxy*-20-*norgibberell*-16-*ene*-17,19-*dioate* **16**.—Sodium hydride (120 mg, 60% in oil, prewashed with light petroleum) in dry THF (15 cm^3) was stirred with a crystal of 18-crown-6-ether for 15 min. The hydroxy compound **15** (80 mg) was added and stirred for 15 min. Carbon disulfide (160 mm^3) was then added and the mixture was stirred for 2.5 h, followed by addition of iodomethane (260 mm^3) with further stirring for 3 h. The resultant mixture was diluted with water (50 cm^3), acidified to pH 2 and extracted with ethyl acetate (3 × 50 cm^3). Evaporation of the solvent under reduced pressure gave a gum which was purified by flash chromatography to give the *title compound* **16** (83 mg) as a yellow gum. NMR spectroscopic analysis showed the α- and β-isomers were in the ratio of 1:1.7; (Found: $M^+ - 107$, 345.2075. $C_{23}H_{32}O_5S_2$ requires $M - 107$, 345.2066); α-isomer δ1.12 (s, 18-H_3), 2.53 (s, SCH_3), 3.14 (d, *J* 9, 6-H), 3.68 and 3.72 (each s, 2 × OCH_3), 4.85 and 4.88 (each br s, 17-H_2), 5.58 (m, 1-H); β-isomer δ1.17 (s, 18-H_3), 2.58 (s, SCH_3), 3.02 (d, *J* 9, 6-H), 3.68 and 3.70 (each s, 2 × OCH_3), 4.88 (br s, 17-H_2) and 6.05 (d, *J* 2, 1-H); *m/z* 420 ($M^+ - 32$, 1%), 345 (10), 313 (59), 286 (21), 285 (100), 253 (13), 225 (85), 197 (6) and 91 (15).

Dimethyl ent-20-*Norgibberell*-16-*ene*-7,19-*dioate* **17**.—The mixture of dithiocarbonates **16** (80 mg) in toluene (6 cm^3) was

heated to reflux under nitrogen with 2,2′-dimethyl-2,2′-azo(propionitrile) and tributyltin hydride (140 μl) for 2 h. The solvent was removed under reduced pressure and the resultant yellow gum was purified by flash chromatography to afford 20-*norgibberellin* A_{12} *dimethyl ester* **17** (50 mg) as a gum (Found: M^+, 346.2141. $C_{21}H_{30}O_4$ requires *M*, 346.2144); δ1.09 (s, 18-H_3), 3.06 (d, *J* 9, 6-H), 3.66 and 3.67 (each s, 2 × OCH_3) and 4.88 (br s, 17-H_2); KRI 2238; *m/z* 346 (M^+, 3%), 314 (37), 287 (17), 286 (57), 254 (23), 227 (73), 226 (100) and 91 (30).

ent-20-*Norgibberell*-16-*ene*-17,19-*dioic acid* **1**.—20-NorGA_{12} dimethyl ester **17** (22 mg) was stirred with sodium propanethiolate–hexamethylphosphoramide (prepared as described previously) (2 cm^3) for 2 d at room temperature, Usual work-up followed by purification by chromatography gave the *diacid* **1** (16 mg) as a white solid which was crystallised from acetone as prisms; m.p. 94–96 °C (Found: $M^+ - 18$, 300.1745. $C_{19}H_{26}O_4$ requires $M - 18$, 300.1725); δ1.17 (s, 18-H_3), 3.11 (d, *J* 9, 6-H) and 4.88 (br, s, 17-H_2); *m/z* 318 (M^+, 0.3%), 300 (69), 274 (4), 272 (100), 275 (17), 228 (11), 221 (50) and 220 (55).

Dimethyl ent-20-*Oxogibberell*-15-*ene*-7,19-*dioate* **19**.—A solution of GA_{24} dimethyl ester **18** (1.5 mg) and iodine (3 mg) in freshly distilled benzene (6 cm^3) was heated to reflux under nitrogen for 20 h. The cooled mixture was washed with aqueous sodium thiosulfate (2 cm^3) and water (5 cm^3). The benzene layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave a gum (1.3 mg). Analysis by NMR spectroscopy and GC–mass spectrometry showed that the resultant mixture consisted of 85% of the required endo-GA_{24} *dimethyl ester* **19**; δ1.18 (s, 18-H_3), 1.59 (br s, 17-H_3), 2.10 (d, *J* 13, 5-H), 3.55 and 3.63 (each s, 2 × OCH_3), 3.80 (d, *J* 13, 6-H), 5.42 (br s, 15-H), 9.62 (br s, 20-H), KRI 2442; *m/z* 346 ($M^+ - 28$, 15%), 314 (100), 286 (98), 271 (16), 243 (25), 227 (69), 178 (20) and 105 (10).

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