Synthesis and structure determination of three new 12β-hydroxy C_{20} gibberellins (GA_{127}, GA_{128} and GA_{129})

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Dedicated to Professor Tony McKervey on the occasion of his 65\textsuperscript{th} birthday

(\textit{received} 24 Feb 03; \textit{accepted} 11 Apr 03; \textit{published on the web} 11 May 03)

Abstract

Three new 12β-hydroxylated C_{20} gibberellins have been isolated from strawberry fruitlets and their structures confirmed by synthesis from gibberellic acid. The key stages in the synthesis involved transannular hydroxylation using diacetoxy iodobenzene and oxidative cleavage of an enolate function by molecular oxygen.

Keywords: Gibberellin, strawberry, transannular hydroxylation, diacetoxy iodobenzene, enolate, oxidative cleavage

Introduction

In a recent study of naturally occurring endogenous gibberellins (“GAs”) in strawberry fruitlets, we discovered a family of 12,13-dihydroxylated C_{20} GAs.\textsuperscript{1} Three of these were identified as the 12α-hydroxy derivatives of GA_{53} \textsuperscript{1}, GA_{44} \textsuperscript{2} and GA_{19} \textsuperscript{3} (Figure 1) by direct comparison with authentic samples and assigned as GA_{123}, GA_{124} and GA_{125}, respectively. Three further GAs were tentatively identified as the corresponding 12β-epimers since they afforded mass spectra that were identical with the equivalent 12α-epimers, but possessed different retention times on GCMS.

![Figure 1](image-url)

\textsuperscript{1} R = Me
\textsuperscript{2} R = CH_{2}OH (19,20-lactone)
\textsuperscript{3} R = CH=O
In order to confirm the putative structures of the 12α-epimers, we had successfully undertaken their synthesis\(^2\) from gibberellic acid (GA\(_3\)) \(^4\) via GA\(_{87}\) methyl ester \(^5\) as indicated briefly in Scheme 1, i.e. the key stages were transannular hydroxylation of C–12\(^3\) followed by introduction of C–20 by means of a copper catalyzed intramolecular cyclopropanation by a 19-diazoacetyl substituent.\(^4\) We had also applied the same strategy to the preparation of the 12β-epimers,\(^2\) and although the GA\(_{19}\) analogue was successfully prepared this way, an unexpected Wagner–Meerwein rearrangement occurred during the last deprotection step for the GA\(_{44}\) and GA\(_{53}\) derivatives. In this paper we describe our efforts to prepare the 12β-hydroxy series by an alternative route that re-orders the major transformations and postpones the 12–hydroxylation step to a later stage of the synthetic sequence (Scheme 2).

Scheme 1
Scheme 2
Results and Discussion

Ketone 16 is reliably available in only 6 steps from GA_4 using the same cyclopropane-based methodology outlined in Scheme 1 and was selected as the substrate for the introduction of the 12β-hydroxyl. Attempts to mask the C-19 carbonyl function as an acetal required fairly vigorous conditions that resulted in partial Wagner–Meerwein rearrangement of the C/D ring system, so instead, the methoxymethyl group was removed from 16, the product reduced with NaBH_4 and acetylated. The stereochemistry at C-19 was established as S from nOe experiments on the intermediate diol, i.e. irradiation of 19-CH (at 4.19 ppm) afforded enhancement of H-6 (doublet, J = 12.0 Hz, at 2.64 ppm). Next, in preparation for the transannular oxidation step (22→23), oxygenation at C-17 was effected by two different approaches: allylic oxidation at C-15 with SeO_2 followed by pyridinium chlorochromate to aldehyde 19 (obtained as a 2:1 mixture with the 15,16-epoxy derivative) and then reduction with Cr(II)Cl_2 to give aldehyde 20 or by treatment of epoxide 18 with dicyclopentadienyl titanium (III) chloride. There was little to choose between the two routes. Bromination of aldehyde 20 afforded a 4:1 mixture of endo and exo aldehydes, and the mixture reduced with NaBH_4, then treated with diacetoxy iodobenzene and iodine while irradiating with a 250W tungsten lamp. Ether 23 was obtained in excellent yield and subjected to a reductive elimination with zinc–HCl to afford the 12β-ol 24. Again, the yield was excellent. After protection of the 12-hydroxyl as a THP ether, and hydrolysis of the two acetate functions, the C-19 carbonyl group was re-established (Dess–Martin periodinane) and oxidative cleavage of the C19–C20 bridge effected by oxygenation of the derived potassium enolate.

The product from this last step is a carboxy aldehyde in equilibrium with the hydroxy lactone with a rate constant similar to that of the NMR time scale, so NMR spectra were poor (compounded by the diastereomeric THP groups). A sample was therefore methylated with diazomethane for characterization purposes. Removal of the THP group then revealed the dimethyl ester of 12β-hydroxy GA_19 (now assigned as GA_129), identical with the sample prepared previously. Reduction of 26 with NaBH_4 readily furnished the GA_44 analogue (= GA_128), but Wolff–Kishner reduction of 26, 28 or the corresponding dicarboxylic acid completely failed under conditions that have been successfully employed on GA_19 and several of its derivatives. 12β-hydroxy-GA_53 (GA_127) was subsequently prepared by applying the 12β-hydroxylation protocol to GA_53, however. With these three reference samples in hand, we were able to confirm by direct comparison (GCMS) the identity of the new strawberry GAs as tentatively assigned. 12-epi-GA_77 30 was also identified as an endogenous GA by direct comparison with an authentic sample and is assigned as GA_130. It is tempting to speculate, as with the 12α,13-dihydroxy GA series, that this collection of 12β-hydroxy GAs constitutes an early 12β,13-dihydroxylation biosynthetic pathway, but we suspect that in both cases it is more likely a consequence of indiscriminate hydroxylation by a C-12 dioxygenase.
With these four GAs, the total of GAs isolated from strawberry fruit has reached 26, of which seven are new. Further novel GAs have also been isolated from this source and we will report on progress towards the determination of their structures shortly. This alternative approach to the synthesis of 12-hydroxy C\textsubscript{20} GAs is somewhat more efficient in terms of individual yields, but the sequence is similar in length to those of the earlier efforts.\textsuperscript{2}

**Experimental Section**

**General Procedures.** Infrared spectra (\(\nu_{\text{max}}\) cm\(^{-1}\)) were recorded on a Perkin–Elmer 1800 Fourier Transform Infrared spectrometer or a Perkin–Elmer 683 Infrared Spectrometer using NaCl or KI plates. \(^1\)H NMR were recorded on either a Varian Gemini 300 MHz or Varian VXR500 MHz instrument and \(^13\)C NMR were recorded on either a Varian Gemini 300 MHz or Varian VXR500 MHz instrument. Chemical shifts are reported as values in parts per million (\(\delta\) ppm). For proton spectra recorded in chloroform, the residual peak of CHCl\(_3\) was used as the internal reference (7.26 ppm) while the central peak of CDCl\(_3\) (77.0 ppm) was used as the reference for \(^13\)C spectra. Multiplicities are abbreviated: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants are recorded in Hertz (Hz). When THP protecting groups have been utilized integrations relate to individual diastereomers; where peaks are superimposed integrations indicate the sum of both diastereomers. Thus a single methyl peak for the mixture integrates to 6H. Assignment has been made where possible with the anomeric protons of the diastereomers and designated as: THP-H1 and THP-H1' in \(^1\)H NMR. Similarly, in the \(^13\)C NMR, where possible, the anomeric carbon is assigned as: THP-C1 and THP-C1'. The remaining protons associated with the THP protecting group have been designated as 'THP' where possible. Distortionless enhancement by polarisation transfer (DEPT) and attached proton test (APT) experiments were used in the assignment of carbon spectra. Low resolution EI mass spectra (EIMS, 70 eV) were recorded on a VG Micromass 7070F double focussing mass spectrometer. Analytical thin layer chromatography (tlc) was conducted on Merck aluminium backed tlc sheets with silica gel 60 F\(_{254}\) or Merck glass backed tlc plates coated with 0.2 mm thick silica gel GF\(_{254}\). The developed plates were visualized under shortwave ultraviolet light and exposed to an ammonium molybdate dip combined with heat. All flash chromatography was carried out using the flash technique as reported by Still\textsuperscript{14} using Merck Kieselgel 60 and analytical reagent (AR) grade solvents as indicated.
Methyl ent-13-hydroxy-19-oxo-19,20-cyclogibberell-16-en-7-oate. A mixture of ketone 16 (4.12 g, 0.011 mmol) and wet Dowex H\(^+\)/50W (12.4 g) in MeOH/H\(_2\)O (120:24 mL) was heated at reflux, 84°C, for 2.5 hours. By this time, all of the starting material had reacted by TLC and the reaction mixture was filtered through a sintered funnel, diluted with EtOAc (100 mL) and NaOAc was added until the pH was ~ 7. The solvent was removed under reduced pressure and the residue was taken up in EtOAc (200 mL). The aqueous phase was extracted with EtOAc (2 × 100 mL) and the combined organic extracts were washed with brine, dried over MgSO\(_4\), filtered and the solvent removed under reduced pressure to afford the title alcohol (3.73 g, 98%) as a white amorphous solid. Purification of the product was not necessary. 

\[1H\text{ NMR (300 MHz, CDCl}_3\text{) }\delta 0.90 (3H, s, H18), 1.38–1.74 (10H, m), 1.81–1.90 (3H, m), 1.91–2.11 (4H, m), 2.22 (1H, dd, } J_{\text{gem}} = 15.8 \text{ Hz, } J = 2.2 \text{ Hz, H15}), 2.37 (1H, dd, } J_{5,6} = 12.0, 1.3 \text{ Hz, H5), 2.43 (1H, dd, } J_{6,5} = 11.9 \text{ Hz, H6), 3.60 (3H, s, CO}_2\text{CH}_3\text{), 4.93 (1H, s, H17), 5.24 (1H, d, } J = 3.1 \text{ Hz, H'}17).\]

\[13C\text{ NMR (75 MHz, CDCl}_3\text{) }\delta 16.6 (\text{CH}_3, \text{C18), 19.4, 19.5 (CH}_2, \text{C2, C11), 36.1 (CH}_2, \text{C20), 37.6, 38.5 (CH}_2, \text{C3, C12), 43.1 (CH}_2, \text{C1), 43.7 (CH}_2 \times 2, \text{C14, C15), 48.4, 48.5 (C, C4, C10), 51.3 (CH}_3, \text{CO}_2\text{CH}_3\text{), 51.7 (CH, C6), 53.1 (C, C8), 54.1 (CH, C9), 59.0 (CH, C5), 77.7 (C, C13), 106.2 (CH}_2, \text{C17), 157.4 (C, C16), 173.0 (C, C7), 220.0 (C, C19). IR } \nu_{\text{max}} \text{ (cm}^{-1}\text{): 3453 (br), 2933, 2869, 1732, 1659. MS (EI) } m/z 344 (M^+, 100%), 312 (69), 285 (74), 135 (62), 91 (43). HRMS (EI) m/z calcd for M^+, C\(_{21}\)H\(_{28}\)O\(_4\): 344.1988; found: 344.1990.\]

Methyl ent-13,19-dihydroxy-19,20-cyclogibberell-16-en-7-oate. A solution of the ketone prepared above (2.11 g, 6.12 mmol) in MeOH (anhydrous, 61 mL) at 0°C was treated with finely ground NaBH\(_4\) (347 mg, 9.19 mmol). The reaction was monitored by TLC analysis and was complete in 10 minutes. After diluting the reaction mixture with EtOAc (100 mL) the entire mixture was washed with K\(_2\)HPO\(_4\) (20% aqueous solution, 50 mL). The aqueous layer was further extracted with EtOAc (2 × 100 mL) and the combined organic extracts were washed with brine, dried over MgSO\(_4\), filtered and the solvent removed under reduced pressure. The residue was chromatographed (silica gel, EtOAc/petrol 3:1) to afford the title alcohol quantitatively (2.15 g) as a white amorphous solid. R\(_f\) 0.4 (EtOAc/petrol 3:1). 

\[1H\text{ NMR (300 MHz, CDCl}_3\text{) }\delta 0.87 (3H, s, H18), 1.18–1.33 (2H, m), 1.45–1.83 (10H, m), 1.70 (1H, d, } J = 9.7 \text{ Hz), 1.89–2.23 (7H, m), 2.64 (1H, d, } J_{6,5} = 12.0 \text{ Hz, H6), 3.68 (3H, s, CO}_2\text{CH}_3\text{), 4.10 (1H, m, H19), 4.88 (1H, s, H17). IR } \nu_{\text{max}} \text{ (cm}^{-1}\text{): 3292 (br), 2941, 1740, 1658. MS (EI) } m/z 346 (M^+, 100%), 314 (91), 286 (74), 135 (62), 91 (43). HRMS (EI) m/z calcd for M^+, C\(_{21}\)H\(_{30}\)O\(_4\): 346.2148; found: 346.2147.\]

Methyl ent-13,19-diacetoxy-19,20-cyclogibberell-16-en-7-oate (17). The diol prepared above (2.15 g, 6.12 mmol) was taken up in DCM (62 mL). After the addition of DMAP (catalytic) the solution was cooled to 0°C then Et\(_3\)N (4.32 mL, 0.031 mmol) was added followed by dropwise addition of Ac\(_2\)O (2.93 mL, 0.031 mmol). The reaction mixture was allowed to warm to room temperature and stirred overnight, by which time the reaction was complete. Ice was then added...
to the reaction mixture and after stirring for 30 minutes the mixture was diluted with EtOAc (100 mL) and HCl (1M aqueous solution, 80 mL) was added. The aqueous phase was extracted with EtOAc (3 x 100 mL) and the combined organic extracts were washed with H2O (100 mL) and brine. After being dried over MgSO4 and filtered, the solvent was removed under reduced pressure to give the desired diacetate 17 (2.59 g, 97%) as a white amorphous solid. Rf 0.5 (EtOAc/petrol 1:3). 1H NMR (300 MHz, CDCl3) δ 0.80 (3H, s, H18), 1.11–1.31 (3H, m), 1.42–1.71 (8H, m), 1.89–2.06 (4H, m), 1.97 (3H, s, OCOCH3), 2.01 (3H, s, OCOCH3), 2.30 (3H, m), 2.65 (1H, d, J5.6 = 12.0 Hz, H6), 3.63 (3H, s, CO2CH3), 4.85 (1H, dd, J = 14.3, 3.9 Hz, H19), 4.88 (1H, s, H17), 5.09 (1H, s, H’17). 13C NMR (75 MHz, CDCl3) δ 19.3, 19.5 (CH2, C2, C11), 20.8, 21.7 (× 2) (CH3, C18, OCOCH3 × 2), 35.4 (CH2, C20), 36.4, 36.8, 37.9 (CH2, C1, C3, C12), 40.0 (CH2, C14), 43.2 (CH2, C15), 44.6, 49.4 (C, C4, C10), 50.3 (CH, C6), 51.3 (CH3, CO2CH3), 51.9 (C, C8), 54.9 (CH, C9), 61.0 (CH, C5), 79.4 (CH, C19), 84.5 (C, C13), 106.9 (CH2, C17), 154.5 (C, C16), 169.6, 170.8 (C, OCOCH3), 173.5 (C, C7). IR νmax (cm−1): 2948, 2871, 1737, 1662, 1243. MS (EI) m/z 430 (M+, 9%), 388 (74), 370 (100), 328 (38), 310 (73), 283 (60), 268 (34), 251 (32). HRMS (EI) m/z calcd for M+, C23H34O6: 430.2355; found: 430.2354.

**Methyl ent-13,19-diacetoxy-16β,17-epoxy-19,20-cyclogibberellane-7-oate (18).** A solution of diacetate 17 (4.36 g, 0.010 mmol) in DCM (150 mL) cooled to −15°C was treated with a solution of m-CPBA (4.36 g of 60%, 0.015 mmol) in DCM (100 mL). The mixture was stirred at −15°C for 30 minutes and the allowed to warm to 4°C and stirred overnight. NaHCO3 (saturated aqueous solution, 100 mL) was added and the reaction mixture stirred for a further 30 minutes. The aqueous phase was extracted with DCM (2 x 100 mL) and the combined organic extracts were washed with H2O (100 mL) and the combined organic extracts were washed with brine, dried over MgSO4 filtered, and the solvent removed under reduced pressure. The residue was chromatographed (silica gel, EtOAc/petrol 1:3) to afford the desired title alcohol (1.20 g, 87%) as a white amorphous solid. Rf 0.6 (EtOAc/petrol 1:3). 1H NMR (300 MHz, CDCl3) δ 0.86 (3H, s, H18), 1.16 (1H, dd,
$J_{gen} = 16.9 \text{ Hz}, J = 2.9 \text{ Hz}$, 1.23–1.35 (2H, m), 1.40 (1H, d, $J = 8.8 \text{ Hz}$), 1.50–1.89 (8H, m), 2.02 (3H, s, OCOCH$_3$), 2.05 (3H, s, OCOCH$_3$), 2.15 (1H, d, $J = 11.3 \text{ Hz}$, H20), 2.14–2.34 (2H, m), 2.57 (1H, d, $J_{6,5} = 12.0 \text{ Hz}$, H6), 2.88 (1H, d, $J = 11.2 \text{ Hz}$, H’20), 3.64 (3H, s, CO$_2$CH$_3$), 3.75 (1H, d, $J_{OH,15B} = 7.5 \text{ Hz}$, 15–OH), 3.95 (1H, d, $J_{15B,OH} = 8.3 \text{ Hz}$, H15), 4.88 (1H, dd, $J = 10.7, 3.9 \text{ Hz}$, H19), 5.14 (1H, s, H17), 5.34 (1H, s, H’17). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 18.7, 19.7 (CH$_2$, C2, C11), 21.1, 21.7, 22.1 (CH$_3$, C18, OCOCH$_3 \times 2$), 35.6, 35.8, 37.6 ($\times 2$), 38.1 (CH$_2$, C1, C3, C12, C14, C20), 45.1 (C), 48.2 (CH, C6), 51.2 (CH, C9), 51.8 (CH$_3$, CO$_2$CH$_3$), 52.4 (C), 56.4 (C, C8), 61.5 (CH, C5), 78.0 (CH, C15), 79.8 (CH, C19), 83.1 (C, C13), 112.3 (CH$_2$, C17), 156.2 (C, C16), 170.9, 171.4 (C, OOCOCH$_3$), 174.7 (C, C7). IR $\nu_{\text{max}}$ (cm$^{-1}$): 3487, 1729, 1645, 1250. MS (EI) $m/z$ 446 (M$^+$, 9%), 414 (23), 326 (100), 266 (84). HRMS (EI) $m/z$ calc d for M$^+$, C$_{25}$H$_{34}$O$_7$: 446.2305; found: 446.2309.

Methyl ent-13,19-diacetoxy-17-oxo-19,20-cyclogibberell-15-en-7-oate (19) and methyl ent-13,19-diacetoxy-15$q$,16$q$-epoxy-17-oxo-19,20-cyclogibberellan-7-oate. A finely ground mixture of PCC (3.02 g, 0.014 mmol) and SiO$_2$ (3.02 g, mass equivalent to PCC) was added to a solution of the allylic alcohol prepared above (2.09 g, 4.68 mmol) in DCM (100 mL) and the suspension was sonicated for 9 hours. Ether (100 mL) was added to the reaction mixture and the mixture was then filtered through a pad of celite which was washed thoroughly with ether (100 mL). The solvent was removed under reduced pressure and the residue was chromatographed (silica gel, EtOAc/petrol 1:2) to afford a mixture (1.51 g, 72%) as a white amorphous solid. A finely ground mixture of PCC (3.02 g, mass equivalent to PCC) was added to a solution of the allylic alcohol prepared above (2.09 g, 4.68 mmol) in DCM (100 mL) and the suspension was sonicated for 9 hours. Ether (100 mL) was added to the reaction mixture and the mixture was then filtered through a pad of celite which was washed thoroughly with ether (100 mL). The solvent was removed under reduced pressure and the residue was chromatographed (silica gel, EtOAc/petrol 1:2) to afford a mixture (1.51 g, 72%) as a white amorphous solid.

Methyl ent-13,19-diacetoxy-17-oxo-19,20-cyclogibberell-15-en-7-oate (19) and methyl ent-13,19-diacetoxy-15$q$,16$q$-epoxy-17-oxo-19,20-cyclogibberellan-7-oate. A finely ground mixture of PCC (3.02 g, 0.014 mmol) and SiO$_2$ (3.02 g, mass equivalent to PCC) was added to a solution of the allylic alcohol prepared above (2.09 g, 4.68 mmol) in DCM (100 mL) and the suspension was sonicated for 9 hours. Ether (100 mL) was added to the reaction mixture and the mixture was then filtered through a pad of celite which was washed thoroughly with ether (100 mL). The solvent was removed under reduced pressure and the residue was chromatographed (silica gel, EtOAc/petrol 1:2) to afford a mixture (1.51 g, 72%) as a white amorphous solid.
OCOCH₃), 2.07 (3H, s, OCOCH₃), 1.84–2.25 (3H, m), 1.88 (1H, d, J_gem = 11.0 Hz, H14α), 2.28 (2H, d, J_gem = 11.0 Hz, H14β), 2.69 (1H, d, J₆,₅ = 12.1 Hz, H6), 3.02 (1H, dd, J = 12.0, 3.8 Hz), 3.69 (3H, s, CO₂CH₃), 4.88 (1H, dd, J = 10.9, 4.3 Hz, H19), 9.98 (1H, s, H17). ¹³C NMR (75 MHz, CDCl₃) δ 19.0, 19.5 (CH₂, C2, C11), 20.9, 21.5. 21.8 (CH₃, C18, OCOCH₃ × 2), 30.1 (CH₂, C12), 35.3, 35.5, 36.7, 37.9 (CH₂, C1, C3, C14, C20), 43.3 (CH₂, C15), 44.7, 49.7 (C, C4, C10), 51.0, 51.4 (CH, C6, C9), 52.0 (C, C8), 55.7 (CH, C5), 57.9 (CH₃, CO₂CH₃), 60.7 (CH, C16), 79.4 (CH, C19), 85.5 (C, C13), 170.2, 171.0 (C, OCOCH₃), 173.4 (C, C7), 201.9 (CH, C17). IR ν_max (cm⁻¹): 1730 (br), 1240. MS (EI) m/z 445 (M+H⁺, 9%), 415 (M⁺–CH₃O, 15), 386 (87), 358 (98), 326 (87), 298 (100), 271 (46), 256 (62), 227 (70), 185 (33), 145 (35), 131 (32), 105 (44), 81 (83). HRMS (EI) m/z calc'd for M⁺–CH₃O, C₂₄H₃₁O₆: 415.2121; found: 415.2118.

**Methyl 16-bromo-13,19-diacectoxy-17-oxo-19,20-cyclogibberellan-7-oate (21).** (a) A solution of aldehyde 20 (3.07 g, 7.32 mmol) in THF (146 mL) was treated with pyrrolidone.HBr (3.9 mL) also at –10°C and the reaction was monitored by TLC analysis. After 20 minutes PHT, the reaction mixture was poured onto ice cold HCl (2M aqueous solution, 10 mL) and stirred for 30 minutes. This was then transferred via cannula into a solution of the α-epoxide (176 mg, 0.394 mmol) in THF (3.9 mL) also at –10°C and the reaction was monitored by TLC analysis. After 20 minutes PHT (585 mg, 1.18 mmol) was added. The reaction mixture was then allowed to warm to room temperature and stirred for 30 minutes. By this time the reaction was complete by TLC analysis and the reaction mixture was poured onto ice cold HCl (2M aqueous solution, 10 mL) layered with EtOAc (10 mL). The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic extracts were washed with H₂O (20 mL), Na₂S₂O₃ (saturated aqueous solution, 20 mL), NaHCO₃ (saturated aqueous solution, 10 mL) and brine. After being dried over MgSO₄ and filtered, the solvent was removed under reduced pressure and the residue chromatographed...
(silica gel, EtOAc/petrol 1:2) which afforded the desired mixture of bromo aldehydes 21 and 16-epi-21 (4:1, 148.0 mg, 71%) followed by the alcohol (11.4 mg, 6%) corresponding to aldehyde 20. Rf 0.4 (EtOAc/petrol 1:1). 1H NMR (300 MHz, CDCl3) δ 0.79 (3H, s, H18), 0.92 (1H, dq, J = 12.9, 2.3 Hz, H11), 1.13 (1H, dd, Jgem = 14.8 Hz, J = 2.6 Hz, H15), 1.19–1.30 (2H, m), 1.44–1.72 (8H, m), 1.81 (1H, d, J5,6 = 11.2 Hz, H5), 1.93–2.08 (3H, m), 1.98 (3H, s, OCOCH3), 2.02 (3H, s, OCOCH3), 2.20–2.36 (3H, m, H16 + 2), 2.62 (1H, d, J6,5 = 12.0 Hz, H6), 3.52 (1H, dd, Jgem = 11.2 Hz, J17,16 = 6.0 Hz, H17), 3.65 (3H, s, CO2CH3), 3.77 (1H, dd, Jgem = 12.0 Hz, J17,16 = 9.3 Hz, H'17), 4.7 (1H, br s, OH), 4.85 (1H, dd, J = 10.7, 3.8 Hz, H19). 13C NMR (75 MHz, CDCl3) δ 19.3, 19.6 (CH2, C2, C11), 21.0, 21.9, 22.1 (CH3, C18, OCOCH3 × 2), 27.6 (CH2, C12), 35.6 (CH2, C20), 36.8, 38.2 (CH2, C1, C3), 39.6 (CH2, C14), 43.6 (CH2, C15), 44.8 (C), 48.2 (CH, C16), 49.8 (C), 51.3 (CH, C6), 51.6 (CH3, CO2CH3), 52.3 (C, C8), 57.2 (CH, C9), 60.9 (CH, C5), 63.2 (CH2, C17), 79.6 (CH, C19), 86.6 (C, C13), 171.1, 171.3 (C, OCOCH3), 173.9 (C, C7). IR νmax (cm⁻¹): 3451, 2950, 1731, 1574. MS (EI) m/z 448 (M⁺, 2%), 388 (90), 347 (61), 328 (71), 287 (100), 269 (36), 227 (71). HRMS (EI) m/z calcd for M⁺–60, C23H32O5: 388.2250; found: 388.2250.

Methyl ent-16β-bromo-13,19-diacetoxy-17-hydroxy-19,20-cyclogibberellan-7-oate (22). Bromo aldehyde mixture 21 plus 16-epi-21 (1.04 g, 1.98 mmol) was taken up in DME (50 mL) and the solution cooled to 0°C. Finely ground NaBH4 (112.3 mg, 2.97 mmol) was added and the suspension stirred for 30 minutes by which time TLC analysis indicated that all of the starting material had been consumed. The reaction mixture was diluted with EtOAc (50 mL) and HCl (1M aqueous solution) was added in a dropwise fashion until all of the remaining NaBH4 was quenched. The aqueous phase was re-extracted with EtOAc (2 × 100 mL) and the combined organic phases were washed with H2O (3 × 100 mL), brine and dried over MgSO4. After filtration, the solvent was removed under reduced pressure and the crude material was chromatographed (silica gel, EtOAc/petrol 1:2) which afforded a 6:1 mixture of the bromo alcohol 22 with its 16-epimer (0.92 g, 64%). Rf 0.4 (EtOAc/petrol 1:2). 1H NMR (300 MHz, CDCl3) δ 0.81 (3H, s, H18), 1.27–1.31 (5H, m), 1.44–1.71 (7H, m), 1.84–2.10 (4H, m), 2.03 (3H, s, OCOCH3), 2.05 (3H, s, OCOCH3), 2.16–2.29 (2H, m), 2.35 (1H, d, J5,6 = 12.3 Hz, H5), 2.45 (1H, d, Jgem = 11.4 Hz, H14), 2.68 (1H, d, J6,5 = 12.0 Hz, H6), 3.70 (4H, s, CO2CH3 + H17 partly obscured), 3.99 (1H, d, Jgem = 12.9 Hz, H’17), 4.87 (1H, dd, J = 10.4, 3.9 Hz, H19). IR νmax (cm⁻¹): 3450, 1730, 1574.

Methyl ent-16β-bromo-13,19-diacetoxy-12α,17-epoxy-19,20-cyclogibberellan-7-oate (23). The mixture of bromo alcohols 22 (662.9 mg, 1.26 mmol) was taken up in DCM (10 mL) and benzene (30 mL) followed by the addition of PhI(OAc)2 (1.22 g, 3.77 mmol) and I2 (0.894 g, 3.52 mmol), then subjected to photolysis (250W tungsten lamp) for 45 minutes. The reaction mixture was diluted with EtOAc (50 mL) and washed with Na2S2O3 (saturated aqueous solution, 50 mL). The aqueous phase was re-extracted with EtOAc (2 × 50 mL) and the combined organic extracts were washed with H2O (100 mL), brine, dried over MgSO4 and filtered. The solvent was removed under reduced pressure and any residual benzene was azeotroped with MeOH. The residue was chromatographed (silica gel, EtOAc/petrol 1:2) to afford the desired cyclic bromo
ether 23 (447.1 mg, 81% yield based on pure 22) as a solid. Rf 0.8 (EtOAc/petrol 1:2). 1H NMR (300 MHz, CDCl3) δ 0.82 (3H, s, H18), 1.12–2.18 (11H, m), 1.92 (1H, d, Jgem = 14.7 Hz, H15), 2.05 (3H, s, OCOCH3), 2.09 (3H, s, OCOCH3), 2.23–2.35 (3H, m), 2.54 (1H, Jgem = 11.5 Hz, H14), 2.68 (1H, d, J6,5 = 11.6 Hz, H6), 3.70 (3H, s, CO2CH3), 3.86 (2H, s, H17, H17'), 4.38 (1H, d, J = 2.6 Hz, H12), 4.93 (1H, dd, J = 10.6, 3.8 Hz, H19). 13C NMR (75 MHz, CDCl3) δ 19.4 (CH2), 21.0, 21.3, 21.6 (CH3, C18, OCOCH3 × 2), 26.2 (CH2, C11), 35.6, 36.6, 37.8, 38.3 (CH2, C1, C3, C14, C20), 44.8, 48.9 (C, C4, C10), 51.6 (C, C16), 51.6 (CH3, CO2CH3), 51.7, 52.4 (CH, C6, C9), 55.0 (CH2, C15), 61.5 (CH, C5), 65.6 (C, C8), 75.9 (CH2, C17), 79.5 (CH, C19), 83.2 (CH, C12), 87.9 (C, C13), 170.2, 171.0 (C, OOCCH3), 173.6 (C, C7). IR νmax (cm⁻¹): 1730. MS (El) m/z 464 (M⁺–60, 64%), 445 (M–Br⁺, 10), 385 (100), 265 (30). HRMS (El) m/z calcd for M⁺–Br⁺, C25H32O7: 445.2226; found: 445.2226.

Methyl ent-13,19-diacetoxyl-12α-hydroxy-19,20-cyclogibberell-16-en-7-oate (24). A suspension of activated zinc (1.02 g, 15.7 mmol) in a solution of the cyclic bromo ether 23 (349.9 mg, 0.666 mmol) in DMF (6 mL) was cooled to 0°C. This was followed by dropwise addition of HCl (5 M aqueous solution, 9 mL) and the mixture stirred for 70 minutes. The reaction mixture was then diluted with EtOAc (50 mL) and washed with H2O (50 mL). The aqueous phase was re-extracted with EtOAc (2 × 50 mL) and the combined organic extracts were washed with H2O (20 mL) and brine (20 mL). The organic phase was dried over MgSO4, filtered, and the solvent was removed under reduced pressure. The residue was chromatographed (silica gel, EtOAc/petrol 1:2) to afford the desired alcohol 24 (255.5 mg, 86%) as a white amorphous solid. Rf 0.2 (EtOAc/petrol 1:2). 1H NMR (300 MHz, CDCl3) δ 0.84 (3H, s, H18), 1.17 (1H, dm, Jgem = 13.2 Hz, H14), 1.20–1.34 (2H, m), 1.53–1.96 (9H, m), 1.97–2.16 (3H, m), 2.04 (6H, s, OCOCH3), 2.20–2.28 (2H, m), 2.68 (1H, d, J6,5 = 12.1 Hz, H6), 3.68 (3H, s, CO2CH3), 4.38 (1H, d, J = 6.6 Hz, H12), 4.87 (1H, dd, J = 10.6, 3.9 Hz, H19), 5.21 (1H, br s, H17), 5.24 (1H, br s, H17'), 5.51 (1H, br s, H17'), 5.84 (1H, br s, H17'). 13C NMR (75 MHz, CDCl3) δ 19.6 (CH2, C2), 21.0, 21.8, 21.9 (CH3, C18, OCOCH3 × 2), 30.5 (CH2, C11), 35.5, 36.9, 38.0 (CH2, C1, C3, C20), 41.8 (CH2, C14), 43.9 (CH2, C15), 44.9, 49.3 (C, C4, C10), 50.4 (CH, C6), 51.6 (CH3, CO2CH3), 51.8 (CH, C9), 51.9 (C, C8), 61.4 (CH, C5), 71.9 (CH, C12), 79.5 (CH, C19), 89.5 (C, C13), 112.8 (CH2, C17), 145.8 (C, C16), 170.7, 171.2 (C, OOCCH3), 173.5 (C, C7). IR νmax (cm⁻¹): 3515, 2950, 1732, 1456, 1076, 1036. MS (EI) m/z 446 (M⁺, 3%), 404 (100), 386 (60), 326 (30). HRMS (El) m/z calcd for M⁺, C25H32O7: 446.2305; found: 446.2303.

Methyl ent-13,19-diacetoxyl-12α-tetrahydropryanyloxy-19,20-cyclogibberell-16-en-7-oate. A solution of alcohol 24 (163 mg, 0.365 mmol) in DCM (5 mL) was treated with dihydropryran (100 μL, 1.09 mmol) and pyridinium p-toluene sulfonate (a few crystals). The mixture was stirred at room temperature overnight. Although TLC analysis indicated that some starting material was still present the reaction mixture was diluted with ether (50 mL) and washed with brine. The aqueous phase was extracted with ether (2 × 10 mL) and the combined organic phases were dried over MgSO4, filtered and the solvent removed under reduced pressure. The residue was chromatographed (silica gel, EtOAc/petrol 1:3) with the desired protected alcohol eluting first (141.3 mg, 90%) as a white amorphous solid, followed by recovered starting material.
Methyl \(\text{ent-13,19-dihydroxy-12\alpha\text{-tetrahydropryanyloxy-19-oxo-19,20-cyclogiberell-16-en-7-oate.}\)}

A suspension of the THP ether prepared above (141.3 mg, 0.266 mmol) and \(\text{K}_2\text{CO}_3\) (anhydrous, 438 mg, 3.17 mmol) in MeOH (anhydrous, 6 mL) was stirred at room temperature for 48 hours. The reaction mixture was diluted with EtOAc (10 mL) and HCl (1M aqueous solution, 3 mL) was added and the mixture stirred for 30 minutes. This was followed by extraction with EtOAc (3 × 30 mL) and the combined organic phases were washed with brine and dried over MgSO\(_4\). After filtration, the solvent was removed under reduced pressure and the residue was then subjected to chromatography (silica gel, EtOAc/petrol 3:1) which afforded the title diol (82.6 mg, 70%) as a white amorphous solid. \(R_f\) 0.4 (EtOAc/petrol 3:1). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 0.83 (6H, s, H18), 1.15–1.41 (5H, m), 1.48–1.91 (28H, m), 1.94–2.23 (10H, m), 2.60 (1H, d, \(J_{6,5} = 11.8\) Hz, H6), 2.61 (1H, d, \(J_{6,5} = 11.8\) Hz, H6), 3.46–3.52 (3H, m, THP), 3.65 (6H, s, CO\(_2\)CH\(_3\)), 3.83–3.89 (2H, m, THP), 3.98–4.12 (6H, H19 + THP), 4.21 (1H, d, \(J = 5.7\) Hz, H12), 4.38 (1H, d, \(J = 5.6\) Hz, H12), 4.85 (2H, s, THP-H1, THP-H1'), 5.12 (2H, s, H17, H'H17). IR \(\nu_{\text{max}}\) (cm\(^{-1}\)) 2945, 1737, 1663, 1239, 1044, 1032, 1021, 755. MS (ES) \(m/z\) 530 (M\(^+\), 4%), 488 (20), 460 (24), 386 (28), 85 (100). HRMS (EI) \(m/z\) calcd for M\(^+\), C\(_{30}\)H\(_{42}\)O\(_8\): 530.2880; found: 530.2888.
1.31–2.09 (38H, m), 2.20–2.38 (7H, m), 3.41–3.51 (4H, m, THP), 3.65 (6H, s, CO$_2$CH$_3$), 3.83–3.89 (1H, m, THP), 4.00–4.08 (2H, m, THP), 4.23 (1H, $t$, $J = 4.4$ Hz, H12), 4.38 (1H, $d$, $J = 5.9$ Hz, H12), 4.82 (1H, m, THP-H1'), 4.95 (1H, s, THP-H1'), 5.15 (2H, s, H17, H'17), 5.20 (1H, s, H17), 5.27 (1H, s, H'17). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 17.0 (CH$_3$, C18 $\times$ 2), 19.7 (CH$_2$ $\times$ 2), 20.3 (CH$_2$), 21.9 (CH$_2$), 24.9 (CH$_2$, C11), 25.3 (CH$_2$, C11), 29.9 (CH$_2$), 30.0 (CH$_2$), 30.6 (CH$_2$), 31.3 (CH$_2$), 36.4 (CH$_2$ $\times$ 2), 37.9 (CH$_2$ $\times$ 2), 43.4 (CH$_2$ $\times$ 2), 43.9 (CH$_2$), 44.2 (CH$_2$), 44.6 (CH$_2$), 45.8 (CH$_3$), 48.9 (C), 49.0 (C), 49.1 (C), 51.5 (C), 51.7 (CH; CH$_3$, CO$_2$CH$_3$), 51.8 $\times$ 2 (CH; CH$_3$, CO$_2$CH$_3$), 51.9 (CH), 52.0 (CH), 53.7 (C $\times$ 2), 59.5 (CH), 59.6 (CH), 63.6 (CH$_2$, THP), 66.0 (CH$_2$, THP), 79.2 (C, C13), 79.7 (CH, C12), 82.2 (C, C13), 84.8 (CH, C12), 100.5 (CH, THP-C1), 101.9 (CH, THP-C1'), 111.8 (CH$_2$, C17), 113.2 (CH$_2$, C17), 148.8 (C, C16), 149.5 (C, C16), 173.2 (C, C7), 173.3 (C, C7), 220.0 (C, C19), 220.1 (C, C19). IR $\nu$$_{max}$ (cm$^{-1}$): 3540, 1750, 1730, 1660. MS (ES) $m$/z 483 (M+K$^+$, 10%), 467 (M+Na$^+$, 73), 445 (M+H$^+$, 52). HRMS (EI) $m$/z calc'd for M$^+$, C$_{26}$H$_{36}$O$_6$: 444.2512; found: 444.2529.

**ent-12α-Tetrahydropyranloxy-13,20,20-trihydroxygibberell-16-en-7,19-dioic acid 19,20-lactone 7-methyl ester (26).** A solution of ketone 25 (46.8 mg, 1.05 mmol) and dry KH (large excess, prepared by washing 3 x with petrol 60–80°C while under nitrogen and then putting under vacuum for 10 minutes) in DMF (dry, 2.7 mL) was degassed by evacuating under high vacuum and re-filling with N$_2$ (3x). THF (2.7 mL) was added and the mixture was cooled to 0°C and stirred for 2 hours. The mixture was then degassed by evacuating under high vacuum and re-filling with N$_2$ (3x) before O$_2$ was bubbled through the reaction mixture for 1 hour. The reaction was purged with N$_2$, then quenched with MeOH (5 mL) and the solvent was removed under reduced pressure. The residue was taken up in EtOAc (10 ml), washed with H$_2$O (2 x 10 mL) and the aqueous layer then re-extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with K$_2$PO$_4$ (20% aqueous solution, 10 mL), brine, and dried over MgSO$_4$. After filtration, the solvent was removed under reduced pressure to afford hydroxy lactone 26 (48.3 mg, 97% yield, crude) which was characterized as the dimethyl ester of the tautomeric aldehyde. A portion of 26 (20 mg) was taken up in MeOH and treated with CH$_2$N$_2$ (1 mL) for 30 minutes. The excess CH$_2$N$_2$ was evaporated under a stream of N$_2$ and the residue was chromatographed (silica gel, EtOAc/petrol 1:1) which afforded the desired dimethyl ester 181 (9.0 mg). $R_f$ 0.66, 0.60 (EtOAc/petrol 1:1). 1H NMR (300 MHz, CDCl$_3$) $\delta$ 1.10 (3H, s, H18), 1.12 (3H, s, H18), 0.85–2.43 (36, m), 3.51 (3H, m, THP), 3.60–3.78 (5H, m, THP), 3.68 (3H, s, COCH$_3$), 3.69 (3H, s, CO$_2$CH$_3$), 3.73 (6H, s, CO$_2$CH$_3$), 3.89 (3H, m, THP), 4.02 (2H, dm, $J = 11.7$ Hz, THP), 4.35 (1H, d, $J = 7.6$ Hz, H12), 4.71 (2H, m, THP-H1, THP-H1'), 5.10 (3H, s, 2 x H17, H'17), 5.17 (1H, s, H'17), 9.75 (1H, s, CHO), 9.78 (1H, s, CHO). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 23.0 (CH$_2$), 20.7 (CH$_2$), 20.8 (CH$_2$), 21.8 (CH$_2$), 24.8 (CH$_2$), 25.2 (CH$_2$), 26.9 (CH$_2$), 27.5 (CH$_3$, C18), 27.6 (CH$_2$), 27.7 (CH$_3$, C18), 30.7 (CH$_2$), 31.6 (CH$_2$), 33.1 (CH$_2$), 33.3 (CH$_2$), 37.5 (CH$_2$), 37.6 (CH$_2$), 43.3 (C, C4), 43.5 (C, C4), 44.6 (CH$_2$), 44.8 (CH$_2$), 48.1 (CH$_2$), 48.3 (CH$_2$), 48.4 (C), 48.5 (C), 49.0 (CH), 49.1 (CH), 51.7 (CH$_3$, CO$_2$CH$_3$ $\times$ 2), 51.8 (CH$_3$, CO$_2$CH$_3$ $\times$ 2), 56.9 (CH), 57.2 (CH), 57.2 (CH), 57.4 (CH), 60.0 (C), 60.3 (C), 63.9 (CH$_2$, THP), 66.1 (CH$_2$, THP), 77.8 (C, C13), 79.2 (C, C13), 80.9 (CH, C12), 84.7 (CH, C12), 100.7 (CH, THP-C1),
102.0 (CH, THP-CH1), 109.9 (CH2, C17), 110.6 (CH2, C17), 148.7 (C, C16), 149.0 (C, C16), 175.3 (C, OCOCH3 × 2), 176.3 (C, C7), 176.4 (C, C7), 205.1 (CH, C20), 205.3 (CH, C20). IR νmax (cm⁻¹): 3500, 1730, 1660. MS (EI) m/z 492 (M⁺, 6%), 462 (17), 434 (53), 419 (63), 402 (30), 372 (55), 344 (65), 300 (51), 97 (100), 62 (38). HRMS (EI) m/z calcd for M⁺–CH3OH, C26H36O7: 460.2461; found: 460.2461.

**ent-13,20-Dihydroxy-12α-tetrahydropyranoxygibberrell-16-ene-7,19-dioic acid 19,20-lactone 7–methyl ester.** A solution of hydroxy lactone 26 (10 mg, 0.0210 mmol) in anhydrous dimethoxyethane (0.5 mL, distilled from CaH2) was cooled to 0°C. Finely ground NaBH₄ (7.0 mg, 0.071 mmol) was added and the mixture was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc (10 mL), washed with KH₂PO₄ (20% aqueous solution, 5 mL), brine and dried over MgSO₄. Following filtration, the solvent was removed under reduced pressure and the residue was chromatographed (silica gel, EtOAc/petrol 2:1) to afford the desired diol 27 (5.4 mg, 56%), Rf 0.3 (EtOAc/petrol 2:1). ¹H NMR (300 MHz, CDC1₃) δ 1.12 (6H, s, H18), 1.18–2.30 (36H, m), 2.74 (1H, d, J₆,₅ = 12.6 Hz, H6), 2.76 (1H, d, J₆,₅ = 12.5 Hz, H6), 3.52 (3H, t, J = 4.1 Hz, THP), 3.69 (6H, s, CO₂CH₃), 3.88 (3H, m, THP), 3.98 (2H, m, THP), 4.08 (1H, d, J₆,₅ = 12.2 Hz, H20-proS), 4.09 (1H, d, J₆,₅ = 12.2 Hz, H20-proS), 4.17 (2H, m, THP), 4.35 (2H, d, J₆,₅ = 12.1 Hz, H20-proR), 4.39 (2H, t, J = 6.1 Hz, H12), 4.80 (1H, m, THP-H1), 5.00 (1H, s, THP-H1'), 5.16 (2H, s, H17, H'17), 5.21 (1H, s, H17), 5.28 (1H, s, H'17). IR νmax (cm⁻¹): 3500, 1730, 1660. MS (EI) m/z 460 (M⁺, 3%), 149 (22), 85 (44), 62 (100). HRMS (EI) m/z calcd for M⁺, C26H36O7: 460.2461; found: 460.2468.

**ent-12α,13,20-Trihydroxygibberrell-16-ene-7,19-dioic acid 19,20-lactone 7-methyl ester (27).** The lactone prepared above (4.1 mg, 0.010 mmol) was dissolved in THF (667 µL), H2O (167 µL), AcOH (167 µL) and the solution was heated at 62°C for 7 hours. Ether (5 mL) was added and the entire mixture was washed with brine. The aqueous phase was re-extracted with ether (2 × 5 mL) and the combined organic extracts were washed with NaHCO₃ (saturated aqueous solution, 5 mL) and brine. The organic phase was dried over MgSO₄, filtered and the solvent removed under reduced pressure and the residue was chromatographed (silica gel, EtOAc/petrol 2:1) to afford the desired diol 27 (0.2 mg), Rf 0.1 (EtOAc/petrol 2:1). ¹H NMR (500 MHz, CDC1₃) δ 1.12 (3H, s, H18), 1.27–1.34 (2H, m), 1.46–1.79 (6H, m), 1.81 (1H, dd, J = 12.0, 2.7 Hz, H11), 1.85 (1H, dm, J₆,₅ = 11.6 Hz, H14α), 1.92 (1H, d, J₆,₅ = 11.6 Hz, H14β), 1.93–2.10 (3H, m), 2.13 (1H, dt, J₆,₅ = 16.2 Hz, J = 2.9 Hz, H15α), 2.20 (1H, d, J₆,₅ = 12.3 Hz, H5), 2.27 (1H, dm, J₆,₅ = 16.0 Hz, H15β), 2.77 (1H, d, J₆,₅ = 12.3 Hz, H6), 3.71 (6H, s, CO₂CH₃), 4.10 (2H, m, H12; d, J₆,₅ = 11.3 Hz, H20-proS), 4.35 (1H, d, J₆,₅ = 12.3 Hz, J₂₀,l₀ = 2.4 Hz, H20-proR), 5.27 (1H, d, J = 1.9 Hz, H17), 5.28 (1H, d, J = 1.3 Hz, H'17). IR νmax (cm⁻¹): 3500, 1730, 1660. MS (EI) m/z 376 (M⁺, 70%), 344 (56), 316 (68), 286 (51), 253 (35), 167 (45), 121 (89), 91 (100). HRMS (EI) m/z calcd for M⁺, C21H23O₆: 376.1886; found: 376.1882.

**ent-12α,13-Dihydroxy-20-oxogibberrell-16-ene-7,19-dioic acid 7,19-dimethyl ester (28).** The dimethyl ester from 26 (3.1 mg, 6.33 mmol) was dissolved in THF/H₂O/AcOH (400 µL:100 µL:100 µL) and the solution was heated at 62°C for 6 hours. The reaction mixture
was diluted with EtOAc (5 mL) and the entire mixture was washed with H₂O (5 mL). The aqueous phase was re-extracted with EtOAc (2 × 5 mL) and the combined organic extracts were washed with H₂O (2 × 5 mL) and brine. The organic phase was dried over MgSO₄, filtered and most of the solvent removed under reduced pressure upon which H₂O (5 mL) was added and the remainder of the organic solvent removed under reduced pressure and the resulting solution was freeze dried. The desired aldehyde 28 was obtained as a white solid (3.5 mg) and the ¹H NMR spectrum was identical to that previously reported. MS (EI) m/z 406 (M⁺, 43%), 328 (22), 300 (24), 121 (25). HRMS (EI) m/z calcd for M⁺, C₂₂H₃₀O₇: 406.1992; found: 406.1987.

Acknowledgements

We are grateful to Bruce Twitchin for technical support.

References and Notes

¶ Unsaturated Aldehyde 19
§ Epoxy Aldehyde
* Major Diastereomer
† Minor Diastereomer
# Peaks associated with the Major Diastereomer

10. Gibberellins are assigned a number corresponding to their order of discovery according to the protocol established by MacMillan, J.; Takahashi, N. Nature 1968, 217, 170. See also Mander, L. N. Nat. Prod. Rep. 2003, 20, 49 and www.plant-hormones.bbsrc.ac.uk/gainplants/gibberellin_nomenclature.htm. Details of the isolation and structure determination for GA₁₂₇ are reported in Nakayama, M.; Koshioka, M.; Matsui, H.; Ohara, H.; Mander, L. N.; Leitch,


