1β-Hydroxygibberellin A_5. Preparation and Comparison with Gibberellin A_3

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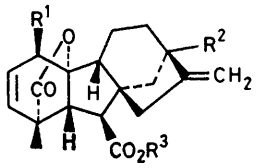
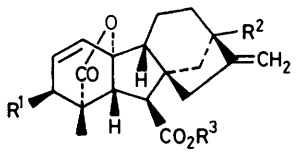
The preparation of 1β-hydroxygibberellin A_5 from gibberellin A_3 is described. Unlike its naturally occurring allylic isomer gibberellin A_3, 1β-hydroxygibberellin A_5 is stable to aqueous alkali and acid-catalysed aromatisation of ring *A* does not occur. Reasons for these differences, and for the hitherto unreported 3-epimerisation of gibberellin A_3 by base, are discussed in terms of *O*-alkyl fission of the lactone bridge.

THE preparation of 1β-hydroxygibberellin A_5 (1) was undertaken for the following reasons. First, following the successful preparation of gibberellin A_{62} (3), and the subsequent identification of this ring-*A*-allylic isomer of gibberellin A_7 (8) in wheat grain and apple seed,[1] an authentic sample of 1β-hydroxygibberellin A_5 (1) was required to determine if this ring-*A*-allylic isomer of gibberellin A_3 (6) occurred naturally in these plant materials. Secondly, it was of interest to compare the stability of the allylic isomers 1β-hydroxygibberellin A_5 (1) and gibberellin A_3 (6) under acidic and basic conditions; insufficient GA_{62} (3) had been prepared [1] for this comparison with gibberellin A_7 (8). Thirdly, since gibberellins A_3 (6) and A_5 (4) show high biological plant-growth-promoting properties,[2] it was of interest to determine the biological activity of 1β-hydroxygibberellin A_5 (1).

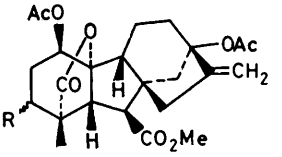


(1) $R^1 = R^2 = OH$, $R^3 = H$
(2) $R^1 = R^2 = OH$, $R^3 = Me$
(3) $R^1 = OH$, $R^2 = R^3 = H$
(4) $R^1 = R^3 = H$, $R^2 = OH$
(5) $R^1 = R^2 = OAc$, $R^3 = Me$

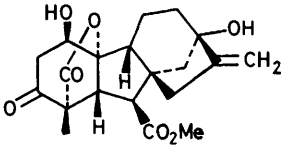


(6) $R^1 = R^2 = OH$, $R^3 = H$
(7) $R^1 = R^2 = OH$, $R^3 = Me$
(8) $R^1 = OH$, $R^2 = R^3 = H$

1β-Hydroxygibberellin A_5 (1) was prepared from gibberellin A_3 (6) in a manner analogous to the preparation of gibberellin A_{62} (3) from gibberellin A_7 (8) (see preceding paper).[1] A mixture of the 3α- and 3β-alcohols (9) and (10) was prepared (preceding paper and ref. 3) from gibberellin A_3 (6) by methylation, oxidation, hydration, acetylation, and reduction. Treatment of this mixture of alcohols with phosphoryl bromide gave a mixture of the 3β-bromo-compound (11), presumably from the 3α-alcohol (9), and the 2-ene (5), presumably from the 3β-alcohol (10). Without separation this mixture of (5) and (11) was treated with 1,5-diazabicyclo[5.4.0]undec-5-ene to give the required 2-ene (5). Mild alkaline hydrolysis of compound (5) with potassium carbonate in methanol gave 1β-hydroxygibberellin A_5 methyl ester (2), identical with one of the products (identified [1] by g.l.c.–mass spectrometry) from the treatment of the *p*-tolylsulphonyl hydrazone of the ketone (12) with sodium cyanoborohydride. Hydrolysis of the methyl ester (2) with potassium hydroxide in aqueous methanol afforded 1β-hydroxygibberellin A_5 (1), which was purified by flash chromatography.[4] In the ^1H n.m.r. spectrum of 1β-hydroxygibberellin A_5 (1) in [$^2H_6$]acetone the 2- and 3-vinylic proton signals were not separated but they were resolved in the spectrum of a [$^2H_5$]pyridine solution, and the spectrum was analogous to that of gibberellin A_3 (6) in the same solvent. The ^{13}C n.m.r. spectrum of 1β-hydroxygibberellin A_5 (1) was likewise analogous to that of gibberellin A_3 (6).

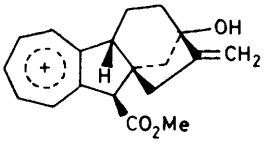


(9) R = α-OH
(10) R = β-OH
(11) R = β-Br



(12)

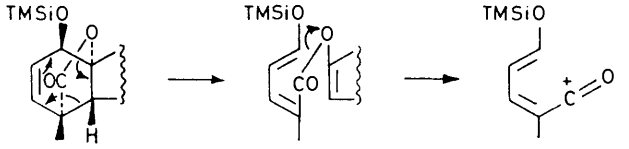
The mass spectra of the two allylic alcohols (1) and (6) and those of their methyl esters, methyl ester trimethyl silyl ethers (MeTMSi derivatives) and trimethylsilyl ester trimethylsilyl ethers (TMSiTMSi derivatives) were similar but distinguishable. The differences reside mainly in fragmentations associated with ring *A*. For example, gibberellin A_3 methyl ester (7) shows an intense



(13)

(80%) peak at $M^+ - 63$, attributable to the aromatic ion (13), which is absent from the spectrum of 1β-hydroxygibberellin A_5 methyl ester (2); this instead contains a peak of moderate intensity at $M^+ - 62$. Also the intense peaks at $M^+ - 122/123$ in the spectrum of gib-

berellin A_3 methyl ester (7) appear at 1 mass unit higher in the spectrum of 1β-hydroxygibberellin A_5 methyl ester (2). In the spectra of the MeTMSi derivatives and TMSiTMSi derivatives, peaks at *m/z* 183 and 387 are intense for the 1β-hydroxygibberellin A_5 derivatives and very weak for the gibberellin A_3 derivatives. The ion at *m/z* 183 has the composition $C_9H_{15}O_2Si$ and may arise from the retro-Diels–Alder process shown in Scheme 1;



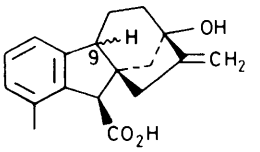
SCHEME 1

a corresponding ion at *m/z* 95 (*i.e.* *m/z* 183 − 88) is present in the spectrum of the MeTMSi derivative of gibberellin A_5 (4) and the same retro-Diels–Alder fragmentation has been proposed [5] for its formation. The ion at *m/z* 387 has the composition $C_{22}H_{35}O_2Si_2$; its origin is not known but must involve the loss of the methoxycarbonyl or trimethylsilyloxycarbonyl group and probably carbon dioxide from the lactone ring; the MeTMSi derivative of gibberellin A_5 (4) shows a corresponding peak at *m/z* 299 of moderate intensity.

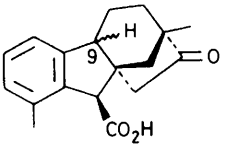
With reference mass spectra of MeTMSi and TMSiTMSi derivatives of 1β-hydroxygibberellin A_5 (1) to hand, the g.l.c.–mass spectrometric data from derivatised extracts of developing wheat grain and apple seed were re-examined. No evidence for the presence of 1β-hydroxygibberellin A_5 (1) in these extracts was obtained.

Interestingly ring *A* in 1β-hydroxygibberellin A_5 (1) is much less reactive than that in gibberellin A_3 (6). Unlike gibberellin A_3 (6), which is transformed into allo- and epiallo-gibberic acids (14) and (15) by treatment with 2M-hydrochloric acid at 50 °C, the allylic isomer is not. In refluxing 2M-hydrochloric acid gibberellin A_3 (6) gives gibberic and epigibberic acids (16) and (17); under these conditions the allylic isomer undergoes rearrangement of rings *C/D*, *without* aromatisation, to give compound (18). These results suggest that the initial step in the ring-*A*-aromatisation of gibberellin A_3 (6) is *O*-alkyl fission of the lactone bridge to give the allylically stabilised ion (19), which then leads, *via* gibberellenic acid (21), to the known products [6] of the acid-catalysed decomposition of gibberellin A_3. In the case of 1β-hydroxygibberellin A_5 (1), *O*-alkyl fission of the lactone is not favoured since the carbocation (20) is not allylically stabilised and, indeed, may be destabilised by the adjacent hydroxy-group. Thus the difference in stabilities of the isomers (1) and (6) is probably a consequence of the difference in the ease of *O*-alkyl fission of the lactone bridge. This point is returned to later.

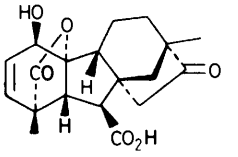
1β-Hydroxygibberellin A_5 (1) and its allylic isomer gibberellin A_3 (6) also differ in their behaviour towards aqueous alkali and heat. Gibberellin A_3 (6) is converted into the isomeric 19,2-lactone (24) both by aqueous alkali (Scheme 2) and thermally during g.l.c. of functional derivatives. In contrast, 1β-hydroxygibberellin A_5 (1) is stable to aqueous alkali and its derivatives can be subjected to g.l.c. without rearrangement. Evidence has



(14) 9α-H
(15) 9β-H



(16) 9α-H
(17) 9β-H



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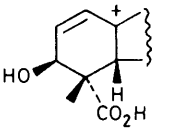

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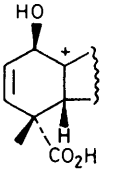

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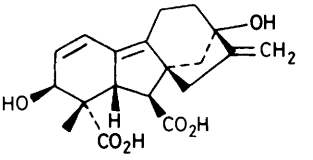


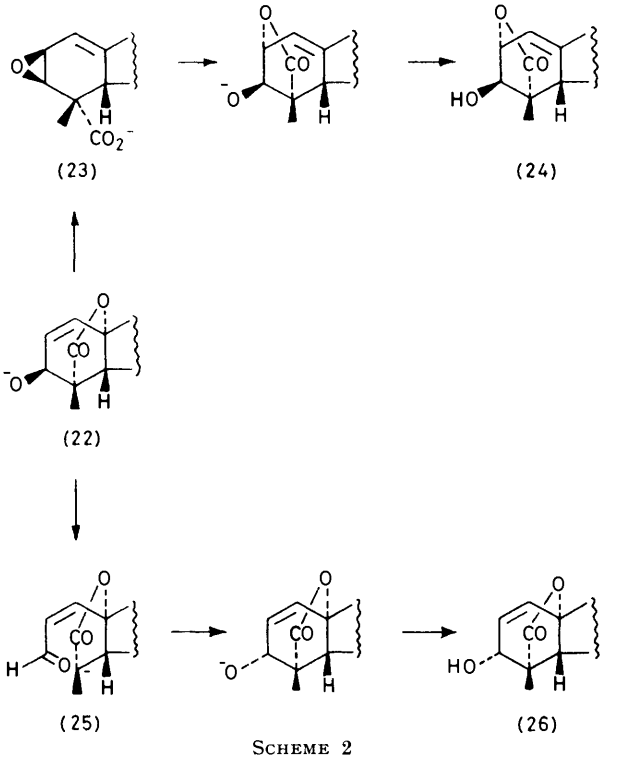
(21)

been presented [7] for the mechanism shown in Scheme 2 whereby an *anti*-S_N2' displacement of the lactone carboxylate by the 3-alkoxide ion (22) gives the intermediate epoxide (23) and hence the 19,2-lactone (24). This mechanism is not available to 1β-hydroxygibberellin A_5 (1) and direct displacement of the lactonic carboxy-group by the 1-alkoxide anion would lead to a highly strained epoxide (27).

As suggested for the acid-catalysed degradation of gibberellin A_3 (6), the base-catalysed isomerisation (6) ⟶ (24) may also be controlled by the ease of *O*-alkyl fission of the lactone bridge. Evidence for this suggestion comes from the observation that when gibberellin A_3 (6) is treated with potassium in t-butyl alcohol, in the absence or presence of small amounts of water, the 3-epimer (26) (Scheme 2) is formed together with the 19,2-lactone (24). Although the epimerisation of saturated ring *A* 3-hydroxygibberellins, such as gibberellin A_1 (28), by dilute aqueous alkali *via* the intermediate aldehyde (29) is well documented,[8-11] the analogous epimerisation of gibberellin A_3 (6) has not been noted previously. However Professor L. N. Mander has informed us that his group † have observed 3-epimerisation in the course of preparing gibberellin A_3

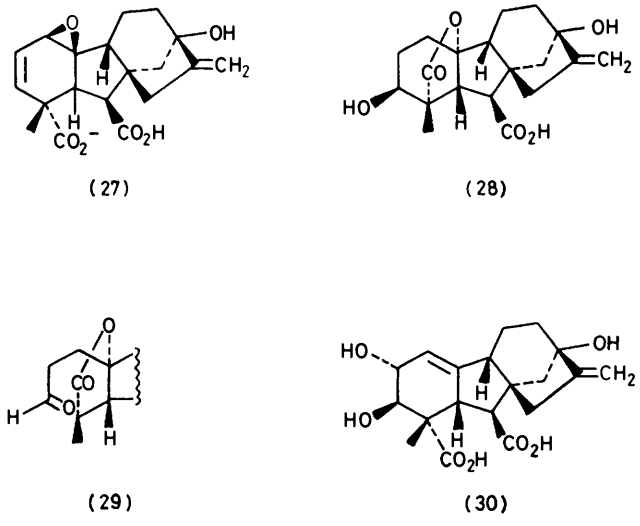
† *Note added in proof:* L. N. Mander and J. V. Turner, *Tetrahedron Lett.*, 1981, **22**, 4149.

methyl ester (7) by a Wittig reaction in t-butyl alcohol. Also, Stork and Singh [12] have reported that brief treatment of the aldehyde (25) (Scheme 2), with 0.01M-sodium ethoxide in ethanol yields a 3 : 1 mixture of gibberellin A_3 (6) and 3-*epi*-gibberellin A_3 (26) (Scheme 2) in 70% yield.



SCHEME 2

As shown in Scheme 2, the 19,2-lactone (24) and 3-*epi*-gibberellin A_3 (26) are the products of competing reactions with the 3-alkoxide (22) as a common intermediate. The alkoxide (22) appears to be in equilibrium with the aldehyde (25) since treatment of gibberellin A_3 (6) with potassium t-butoxide in t-butyl alcohol containing [^{18}O]-water results in the incorporation of oxygen-18 into gibberellin A_3 (6) (7.5% ^{18}O), the 19,2-lactone (24) (5% ^{18}O) and 3-*epi*-gibberellin A_3 (26) (16% ^{18}O). 3-*epi*-Gibberellin A_3 (26), previously shown [7] to be stable to aqueous 0.01M-sodium hydroxide, is also stable in the potassium t-butoxide–t-butyl alcohol–water system. The 19,2-lactone (24) is also stable when re-treated under conditions in which it is formed from gibberellin A_3. From these results it is suggested that the competing reactions in Scheme 2 are controlled by the dielectric constant of the medium in two ways. First, *O*-alkyl fission of the lactone function may be assisted in the more polar aqueous medium leading to the 19,2-lactone (24); secondly, in the less polar medium intramolecular bonding of the 3α-hydroxy-group with the carbonyl of the lactone may favour the formation of 3-*epi*-gibberellin A_3. Stork and Singh [12] have also remarked upon the importance of the dielectric constant of the medium in relation to the reactions of gibberellin A_3 towards alkali.



The biological activity of 1β-hydroxygibberellin A_5 (1) will be reported elsewhere.

EXPERIMENTAL

For general experimental details see ref. 1. Unless stated otherwise mass spectral data were obtained by g.l.c.–mass spectrometry.

ent-1α,13-*Diacetoxy*-10-*hydroxy*-20-*norgibberella*-2,16-*diene*-7,19-*dioic Acid* 7-*Methyl Ester* 19,10-*Lactone* (5).—(*a*) A mixture (1 : 2) (199 mg) of the 3α- and 3β-alcohols (9) and (10), prepared as described previously,[1,3] and phosphoryl bromide (245 mg) in pyridine (5.5 ml) was refluxed in nitrogen for 1 h. Water was added and the pH was adjusted to 3.0 with 10M-hydrochloric acid. Extraction with ethyl acetate gave a gum (220 mg) consisting (n.m.r.) of a mixture (2 : 1) of the 2,3-*olefin* (5) and the 3β-*bromo-compound* (11); δ (for 3β-bromide) 1.23(s, 18-H_3), 2.02(s, 13-OCOMe), 2.15(s, 1β-OCOMe), 2.74(d, *J* 10 Hz, 6-H), 3.18 (d, *J* 10 Hz, 5-H), 3.75(s, CO_2Me), 4.12(br, t, *J* 3 Hz, 3α-H), 4.98(br, s, 17-H), and 5.13(br, s, 17-H and 1α-H); for n.m.r. data of the 2,3-ene (5) see under (*b*).

(*b*) The gum (220 mg) from (*a*) and 1,5-diazabicyclo-[5.4.0]undec-5-ene (0.08 ml) in pyridine (5.5 ml) were refluxed for 1 h in nitrogen. Work-up as in (*a*) and purification of the recovered product by p.l.c. using ethyl acetate–light petroleum (1 : 1) yielded, from R_F 0.55 to 0.65, the 2,3-*olefin* (5) (126 mg), m.p. 155—156.5 °C (from acetone–light petroleum) (Found: C, 64.8; H, 6.2. $C_{24}H_{28}O_8$ requires C, 64.9; H, 6.3%); $\nu_{max.}$ 1 786, 1 729, 1 661, 963, and 903 cm^{-1}; δ 1.23(s, 18-H_3), 2.02(s, 13-OCOMe), 2.12(s, 1β-OCOMe), 2.66 and 3.0 (both d, *J* 10 Hz, 5- and 6-H), 3.75(s, CO_2Me), 5.01 and 5.14(both br, s, 17-H_2), 5.34(d, *J* 3 Hz, 1-H), 5.82(dd, *J* 3 and 9 Hz, 2-H), and 5.97(d, *J* 9 Hz, 3-H); *m/z* (probe) 444(M^+, 4%), 402(25), 298(13), 280(61), 238(36), 221(69), and 43(100).

ent-1α,10,13-*Trihydroxy*-20-*norgibberella*-2,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* 7-*Methyl Ester* (2).—The 2-ene (5) (126 mg) was stirred for 16 h with anhydrous potassium carbonate (120 mg) in methanol (5 ml). Acetic acid (0.35 ml) was added and the methanol was evaporated off. Water was added and the mixture was extracted with ethyl acetate to give 1β-*hydroxygibberellin* A_5 *methyl ester* (2) (101 mg), m.p. 172—174 °C (from ethyl acetate–light petroleum)

(Found: C, 66.8; H, 6.85. $C_{20}H_{24}O_6$ requires C, 66.7; H, 6.7%); $\nu_{max.}$ 3 450, 3 400, 1 791, 1 721, 1 660, and 900 cm^{-1}; δ 1.22(s, 18-H_3), 2.66(d, *J* 10 Hz, 6-H), 2.92(d, *J* 10 Hz, 5-H), 3.74(s, CO_2Me), 4.16(br, s, reduced to d, *J* 2 Hz, on adding D_2O, 1-H), 4.97 and 5.26(both br, s, 17-H_2), and 5.89(s, 2- and 3-H); *m/z* (probe) 360(M^+, 45%), 359(21), 328(100), 301(55), 298(41), 239(100), 238(82), 136(55), 135(55), and 121(52); *m/z* (bis-TMSi ether) 504(M^+, 36%), 489(8), 445(16), 387.220 (32%, $C_{22}H_{35}O_2Si_2$ requires 387.218), 208(34), 193(20), 183.084(64%, $C_9H_{15}O_2Si$ requires 183.084), 75(34), and 73(100).

ent-1α-10,13-*Trihydroxy*-20-*norgibberella*-2,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* (1).—The methyl ester (2) (94 mg) and potassium hydroxide (200 mg) in methanol (5 ml) and water (5 ml) were refluxed for 25 h. After the usual work-up, the neutral portion yielded unchanged methyl ester (2) (19 mg). The acidic extract yielded a gum (22 mg) which was separated by flash chromatography on a column (15 × 2 cm) with acetone–light petroleum–acetic acid (25 : 75 : 1) to give some residual starting material and 1β-*hydroxygibberellin* A_5 (1), which crystallised from ethyl acetate–light petroleum in needles (16 mg), m.p. 220—222 °C, or from ethyl acetate in cubes, m.p. 135—138 °C, resolidifying and remelting at 222—224 °C (Found: M^+, 346.142. $C_{19}H_{22}O_6$ requires *M*, 346.142); $\nu_{max.}$ (tetrahydrofuran) 3 410br, 1 786, 1 729, and 1 656sh cm^{-1}; δ [$(CD_3)_2$-CO] 1.18(s, 18-H_3), 2.57(d, *J* 10 Hz, 6-H), 2.91(d, *J* 10 Hz, 5-H), 4.12(d, *J* 3 Hz, 1-H), 4.91 and 5.22(both br, s, 17-H_2), and 5.89(s, 2- and 3-H); δ_H ([$^2H_5$]pyridine) 1.46(s, 18-H_3), 3.19(d, *J* 10 Hz, 6-H), 3.59(d, *J* 10 Hz, 5-H), 4.48(dd, *J* 0.5 and 3.5 Hz, 1-H), 5.01 and 5.57(both br, s, 17-H_2), 5.94(dd, *J* 0.5 and 9.5 Hz, 3-H), and 6.22(dd, *J* 3.4 and 9.5 Hz, 2-H); δ_C ([$^2H_5$]pyridine) 15.52(q, C-18), 17.60(t, C-11), 40.02(t, C-12), 43.72(t, C-15), 46.45(t, C-14), 47.60 (d, C-9), 49.17(s, C-8),† 49.71(s, C-4),† 51.68(d, C-5), 52.1(d, C-6), 66.04(d, C-1), 77.88(s, C-13), 95.54(s, C-10), 106.59(t, C-17), 132.27 (d, C-3), 134.90(d, C-2), 159.02(s, C-16), 174.84(s, C-7), and 178.48(s, C-19); *m/z* (probe) 346(M^+, 7%), 330(1), 328(8), 301(10), 300(18), 284(85), 239(36), 155(33), 136(29), 121(25), and 44(100).

G.l.c.–mass spectrometry of the TMSi ester TMSi ether showed the presence of 1—2% of the methyl ester. The TMSi ester TMSi ether had *m/z* 562(M^+, 54%), 547(33), 445(49), 387(34), 311(21), 208(22), 207(11), 193(10), 183(46), 75(70), and 73(100).

Treatment of ent-1α,10,13-*Trihydroxy*-20-*norgibberella*-2,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* (1) *with Acid*.—The acid (1) (5 mg) in 2M-hydrochloric acid (9 ml) was refluxed for 1 h. Extraction with ethyl acetate and crystallisation of the extract from ethyl acetate–light petroleum gave the *rearranged compound* (18) in needles (4 mg), m.p. *ca.* 290 °C (decomp.); $\nu_{max.}$ (Nujol) 3 590, 3 360br, 1 750, 1 740, and 1 640br cm^{-1}; $\nu_{max.}$ ($CHCl_3$) 3 100br, 3 040, 2 750br, 1 780, 1 760, and 1 715 cm^{-1}; δ ([$^2H_5$]pyridine) 1.00(s, 13-Me), 1.45(s, 18-H_3), 3.29(d, *J* 6 Hz, 6-H), 3.67(d, *J* 6 Hz, 5-H), 4.56(d, *J* 3 Hz, 1-H), 5.96(d, *J* 9 Hz, 3-H), and 6.14 (dd, *J* 3 and 9 Hz, 2-H); *m/z* (TMSi ester TMSi ether) 490 (M^+, absent), 475(35), 328(20), 239(81), 238(100), 195(15), 155(17), 75(73), and 73(86).

The methyl ester had *m/z* 360(M^+, 1), 329(2), 316(3), 298(16), 239(31), 211(14), 195(13), 155(14), 45(100), and 29(37). The methyl ester TMSi ether had *m/z* 432(M^+, absent), 417 (8%), 388(26), 298(40), 239(96), 238.163 ($C_{17}H_{18}O$ requires 238.136, 100%), 211(29), 195(27), 193(25), 167(21), 155(29), 91(20), 75(64), 73(96), and 44(24).

† Assignments may be interchanged.

Treatment of ent-3α-10,13-*Trihydroxy*-20-*norgibberella*-1,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* (*Gibberellin* A_3) (6) *with Base* (with David A. Taylor).—(*a*) Freshly cut potassium metal (220 mg), washed with light petroleum, was dissolved in dry t-butyl alcohol (100 ml) and water (85 μl). Gibberellin A_3 (6) (200 mg) was added and, after 18 h, acetic acid (20 ml) was added to neutralise the alkali. Evaporation left a solid which was dissolved in water (70 ml). The solution was acidified to pH 3 by adding 3M-hydrochloric acid, then extracted with ethyl acetate (2 × 75 ml), the extract was washed with water (1 × 20 ml) and evaporated to give a foam (150 mg). This foam, which was shown to consist of 30% of the diacid (30) and 70% of 3-*epi*-gibberellin A_3 (26) by ^1H n.m.r., was subjected to flash chromatography on a column (16 × 2 cm) of Kieselgel 60 with the solvent system ethyl acetate–light petroleum–acetic acid (80 : 20 : 1) to give pure 3-*epi*-gibberellin A_3 (26), characterised by comparison of n.m.r. and mass spectra with the literature values.[7]

(*b*) Experiment (*a*) was repeated without water in the reaction mixture. Analysis of the methylated and trimethylsilylated product by g.l.c.–mass spectrometry showed the presence of 3-*epi*-gibberellin A_3 (26) (45%), gibberellin A_3 (6) (4%), and the 19,2-lactone (51%). The yield of the last mentioned compound included that formed by thermal isomerisation of the MeTMSi derivative of gibberellin A_3 (6).

(*c*) Experiment (*a*) was repeated using potassium metal (20 mg), t-butyl alcohol (20 ml), ^{18}O-enriched water (0.0008 ml, 61.1 atoms % ^{18}O), and gibberellin A_3 (6) (20 mg). G.l.c.–mass spectrometric analysis of the MeTMSi derivative of the product showed the presence of gibberellin A_3 (6) (14%) (7.5% ^{18}O), 3-*epi*-gibberellin A_3 (26) (66%) (16% ^{18}O) and the 19,2-lactone (24) (20%) (5% ^{18}O); again the yield of the isomeric lactone (24) includes that produced by thermal rearrangement.

Treatment of ent-3β,10,13-*Trihydroxy*-20-*norgibberella*-1,16-*diene*-7,19-*dioic Acid* 19,10-*Lactone* (26) (3-epi-*Gibberellin* A_3) *with Base* (with David A. Taylor).—3-*epi*-Gibberellin A_3 (26) (85 mg) was dissolved in t-butyl alcohol (50 ml) and water (40 μl). Freshly cut potassium metal (90 mg), washed with light petroleum, was added and the mixture was stirred at room temperature for 21 h. Work-up as in the previous experiment (*a*) gave a yellow gum (70 mg) which was identified as starting material by n.m.r. and g.l.c. No gibberellin A_3 or 19,2-lactone (24) was detected in the product.

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REFERENCES

[1] P. S. Kirkwood and J. MacMillan, preceding paper.
[2] For leading references see D. R. Reeve and A. Crozier in 'Gibberellins and Plant Growth,' ed. H. N. Krishnamoorthy, Wiley Eastern, New Delhi, 1975, pp. 35—64.
[3] P. Gaskin, P. S. Kirkwood, J. R. Lenton, J. MacMillan, and M. E. Radley, *Agric. Biol. Chem.*, 1980, **44**, 1589.
[4] W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
[5] J. R. Bearder, P. S. Kirkwood, and J. MacMillan, *J. Chem. Soc., Perkin Trans. 1*, 1981, 672.

[6] R. J. Pryce, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1179, and references cited therein.
[7] P. S. Kirkwood, J. MacMillan, and M. L. Sinnott, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2117.
[8] B. E. Cross, J. F. Grove, and A. Morrison, *J. Chem. Soc.*, 1961, 2498.
[9] R. H. Cornforth, quoted by B. E. Cross, *Chem. Ind.*, 1959, **78**, 184.
[10] G. Stork and H. Newman, *J. Am. Chem. Soc.*, 1959, **81**, 5518.
[11] J. MacMillan and R. J. Pryce, *J. Chem. Soc. C*, 1967, 740.
[12] G. Stork and J. Singh, *J. Am. Chem. Soc.*, 1979, **101**, 7109.