Partial Synthesis of Gibberellin A_{37} by Selective Reduction of the Hindered 10-Carboxy-group in Gibberellin A_{13}

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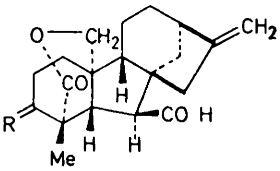
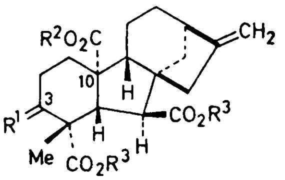
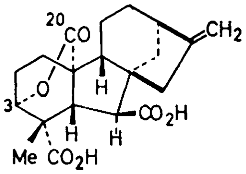
Summary Selective reduction of the severely hindered 10-carboxy-group in gibberellin A_{13} (**5**) has been achieved through its 20 → 3-lactonic derivative (**10**) in which the relevant carbonyl function is made more accessible; a partial synthesis of the new gibberellin A_{37} (**2**) is thus provided.



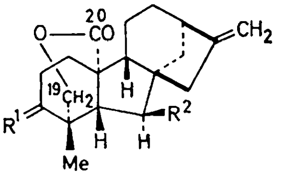
(1) $R = H_2$
(2) $R = H, \beta$-OH
(3) $R = H, \alpha$-OH
(4) $R = O$



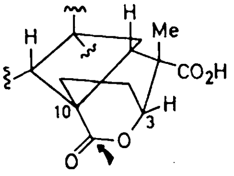
(5) $R^1 = H, \beta$-OH, $R^2 = R^3 = H$
(6) $R^1 = O, R^2 = R^3 = H$
(7) $R^1 = H, \alpha$-OH, $R^2 = R^3 = H$
(8) $R^1 = H, \beta$-OTHP, $R^2 = Me, R^3 = H$
(9) $R^1 = O, R^2 = R^3 = Me$



(10)



(11) $R^1 = O, R^2 = CO_2H$
(12) $R^1 = H, \alpha$-OH, $R^2 = CO_2H$
(13) $R^1 = H, \beta$-OH, $R^2 = CO_2H$



(10a)

The need for a partial synthesis of derivatives of gibberellin A_{15} (GA_{15}) (**1**) from the relatively accessible GA_{13} (**5**) has been cogently argued by Cross and Stewart.[1] A further stimulus has been provided recently[2] by the isolation of the new gibberellin, GA_{37} (**2**), as its β-D-glucosyl ester, from mature seed of *Phaseolus vulgaris*. The challenging step in the conversion of GA_{13} (**5**) into GA_{15} (**1**) and GA_{37} (**2**) is the selective reduction of the highly hindered 10-carboxy-group in GA_{13} (**5**). This selective reduction has now been effected *via* the 20 → 3-lactone (**10**) in which the lactonic carbonyl function is held in an accessible orientation (see **10a**). The following partial synthesis of GA_{37} (**2**) has thus been developed.

The 20 → 3-lactone (**10**) was prepared by reduction ($NaBH_4$) of 3-oxo-GA_{13} (**6**), followed by pyrolysis at 135° of the resultant mixture of the 20 → 3-lactone (**10**) and the hydroxy-acid (**7**). Reduction ($LiBH_4$) of the 20 → 3-lactone (**10**) in tetrahydrofuran at 20° directly gave the 19 → 20-lactone (**3**), oxidised by Jones' reagent to the ketone (**4**). Reduction [$Al(OPr^i)_3$ in Pr^iOH] of the latter compound gave a 1 : 1 mixture of the 3β-(**2**) and 3α-(**3**) epimers which were separated by t.l.c. on silica gel with EtOAc–light petroleum–AcOH (50 : 50 : 1). The faster moving 3β-isomer (**2**) was identical (m.p., g.l.c., and spectroscopic properties) with GA_{37} (**2**), prepared by reduction of GA_{36};[3] the methyl esters were also identical. In the Meerwein–Ponndorf reduction of the isomeric 3-oxo-20 → 19-lactone (**11**) Cross and Stewart[1] obtained mainly the 3α-epimer (**12**) and only traces of the 3β-epimer (**13**) (in our hands 15—20% by g.l.c.). Molecular models indicate that hydride transfer from the α-face in the aluminium isopropoxide–lactone (**11**) complex is impeded by the 19-methylene groups. In the less encumbered 3-oxo-GA_{13}-trimethyl ester (**9**), the 3β-alcohol was found to be the major product.

Thus reduction with aluminium isopropoxide of 3-oxo-gibberellins may only exceptionally yield the unnatural 3α-hydroxy-epimers.

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[1] B. E. Cross and J. C. Stewart, *J. Chem. Soc.* (*C*), 1971, 245.
[2] K. Hiraga, T. Yokota, N. Murofushi, and N. Takahashi, *Agric. Biol. Chem.* (*Japan*), 1972, **36**, 345.
[3] J. R. Bearder and J. MacMillan, *Agric. Biol. Chem.* (*Japan*), 1972, **36**, 342.