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A Partial Synthesis of Gibberellin A_{14}-aldehyde, a Probable Biosynthetic Intermediate of Gibberellins.

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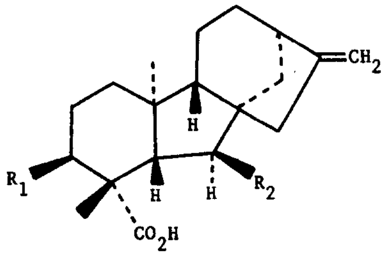
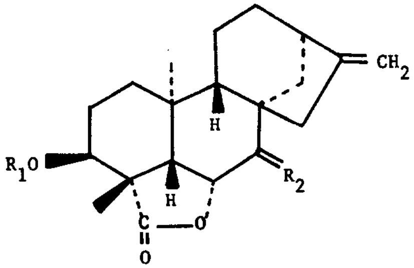
We have recently shown[1] that gibberellin A_{12}-aldehyde (I), a central intermediate in gibberellin biosynthesis,[2,3] is efficiently converted into gibberellin A_{14} (V) by cultures of Gibberella fujikuroi, thus providing direct evidence for the suggestion[3] that 3-hydroxylation precedes lactone formation in C_{19}-gibberellins. Under the same conditions the corresponding di-acid, gibberellin A_{12} (IV), is poorly transformed[1] into gibberellin A_{14} (V), indicating the direct 3-hydroxylation of gibberellin A_{12}-aldehyde (I) and the intermediacy of gibberellin A_{14}-aldehyde (II). We now report the synthesis of this previously unknown aldehyde (II) from the lactone (VI).

The lactone (VI) was recently isolated by Bateson and Cross[4] from G. fujikuroi. We had also isolated[5] this metabolite from the culture filtrates of G. fujikuroi (mutant strain TP70) where it was detected by GC-MS of the trimethylsilylated neutral metabolites and assigned[5] the same structure (VI). However loss of the data and samples by fire (April 1971) prevented earlier publication. Our evidence for structure (VI) which will be detailed in the full paper is essentially the same as that outlined by Bateson and Cross.[4]

Reaction of the lactone (VI) with an equimolar amount of dihydropyran and traces of toluene-p-sulphonic acid gave the required 3-tetrahydropyranyl (THP) ether (VII) in 25-30% yield together with the 7-THP ether (VIII, 20-25%) and the 3,7-diTHP ether (IX, 5-15%). The two mono-THP ethers (VII), m.p. 185-200°, and the gummy (VIII), both diastereoisomeric mixtures, were distinguished by the MS of their TMSi ethers, that from (VIII) showing a strong $^{m}/e$ 129 peak.[6] Quantitative oxidation (CrO_3-pyridine) of the 3-THP ether (VII) to the 7-ketone (IX), m.p. 173-181° ($\nu_{C=O}^{CHCl_3}$ 1783, 1720 cm^{-1}), followed by sodium borohydride reduction (90% yield) gave the 7α-hydroxy isomer (X), tosylation of the latter, followed by heating under nitrogen with potassium hydroxide in t-butanol containing 4% water effected ring contraction in 70% yield to the aldehyde (III). Hydrolysis of the latter by boiling methanol containing 10% acetic acid (nitrogen-atmosphere) completed the synthesis of gibberellin A_{14}-aldehyde (II) m.p. 154-5° (M$^+$ 332.197. $C_{20}H_{28}O_4$ requires M 332.199) [τ-values ($CDCl_3$) 9.22 (4-Me, s), 8.74 (10-Me, s), 7.56 (5-H, d, J 12Hz), 6.78 (6-H, dd, J 12,6Hz), 5.84 (3-H, *m*, $W_{\frac{1}{2}}$ *ca.* 7Hz), 5.16 (17-H, m) and 5.06 (17-H, m), and 0.27 (7-H, d, J 6Hz); ν ($CHCl_3$) 3677 and 3500 br (OH), 3400-2400 (OH of CO_2H), 2730 (CHO), 1710 br (C=O), 1658 and 882 cm^{-1} (C=C)]. Irradiation at τ6.8 caused the collapse of the 5- and 7-protons to singlets.

The metabolism of gibberellin A_{14}-aldehyde (II) is under active study.





	R1	R2		R1	R2
I	H	CHO	IV	H	CO_2H
II	OH	CHO	V	OH	CO_2H
III	OTHP	CHO			

	R1	R2		R1	R2
VI	H	H,β-OH	IX	THP	O
VII	THP	H,β-OH	X	THP	H,α-OH
VIII	H	H,β-OTHP			

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