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THE FORMATION OF THE C_{19}-GIBBERELLINS FROM GIBBERELLIN A_{13} ANHYDRIDE

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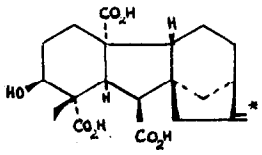
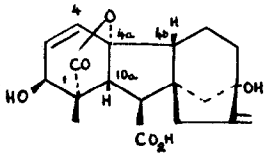
There are two groups of gibberellin plant growth hormone. The C_{20} hormones possess a C-4a angular substituent [CH_3, CH_2OH, CHO (as part of a lactone or a hemi-acetal respectively) or CO_2H] whilst the C_{19} hormones lack this substituent possessing instead a 1 → 4a γ-lactone. Recently the suggestion has been made[1] that the aldehydes may be the immediate precursors of the C_{19} gibberellins. We have shown[2] that mevalonoid hydrogen is retained at C-4, C-4b and C-10a during the formation of the C_{19} gibberellins thus excluding olefinic intermediates from this stage in the biosynthesis and we proposed that lactone formation might involve a Baeyer-Villiger type of oxidation of a carbonyl function. In this context it should be noted that the lactone bridge occupies the same face of the molecule as the C-4a angular substituent. Gibberellin A_{13} (1) has been shown not to be incorporated[3] into gibberellic acid (2).

Gibberellin A_{13} anhydride (3)[4] was a likely candidate for trial as a precursor. It was prepared in the following manner. 7α-Hydroxykaurenolide (4), which is readily available from the fungal metabolite 7β-hydroxykaurenolide,[5] was converted to its p-bromobenzenesulphonate. This was converted to the aldehyde (5) in 76% yield by heating with potassium hydroxide in t-butanol under reflux. The aldehyde was



(1)



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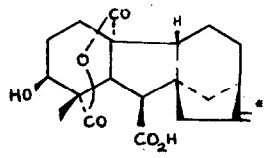

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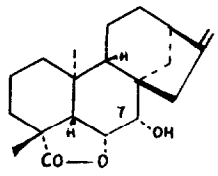

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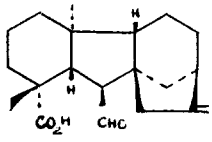

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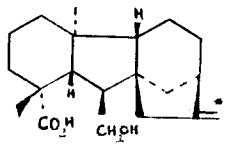

(6)

reduced with sodium borohydride to afford the gibbane alcohol (6) which on ozonolysis in pyridine:carbon tetrachloride at -78°, afforded the corresponding nor-ketone. This was reconverted to the [^{14}C]-gibbane alcohol (6) using [^{14}C]-triphenylphosphonium methiodide and sodium hydride in dimethylsulphoxide. The labelled alcohol was used as a substrate for microbiological conversion to gibberellin A_{13} by the fungus Gibberella fujikuroi . The gibberellin A_{13} was subjected to extensive purification on Sephadex G-25 and preparative layer chromatography. The anhydride (3) was then prepared by controlled pyrolysis.[4] It was however unstable under the conditions of the fermentation reverting over a period of hours to gibberellin A_{13}. Nevertheless [^{14}C]-gibberellin A_{13} anhydride (3) and [^{14}C]-gibberellin A_{13} (1) were fed for 18 hours to identical cultures of the fungus, Gibberella fujikuroi. Although the major amount of the radio-activity from the anhydride appeared in the gibberellin A_{13}, there was a small but significant specific incorporation into gibberellic acid (0·14%) and the gibberellin A_4/A_7 fraction (0·07%). There was no detectable incorporation into these substances from the [^{14}C]-gibberellin A_{13}.

Therefore we suggest that the loss of the angular substituent requires the presence of the 1 - 4a substituent oxygen bridge and that possibly it occurs at the anhydride oxidation level. This implies a unique biosynthetic transannular participation reaction involving the C-1 carboxyl group. In this context it is worth pointing out that the angular alcohols and aldehydes readily interact with this substituent in lactone and hemi-acetal formation. Because of the competing non-enzymatic hydrolysis which may be augmented by transport problems across the cell wall, we are as yet unable to distinguish between a microbiological conversion and a true biosynthesis. Experiments to prepare a cell-free system capable of mediating this step are in hand. Nevertheless we should point out that the fungus occassionally produces large quantities of gibberellin A_{13} at the expense of

gibberellic acid suggesting that in these cases hydrolysis predominates over decarboxylation. Furthermore gibberellin A_{13} was first isolated from a fermentation to which the inhibitor of cholesterol biosynthesis, triparanol, had been added.[4]

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