The Synthesis of Gibberethiones, Gibberellin-related Diterpenoids

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Gibberethione\* isolated from seed of *Pharbitis nil* (Japanese morning glory) is a catabolic product of gibberellin  $A_3$  (GA<sub>3</sub>). Its structure was determined to be III based on X-ray analysis.<sup>1)</sup>

This report deals with the synthesis of gibberethione. As gibberethione is consisted of 3-keto-GA<sub>3</sub> (I) and mercaptopyruvic acid moieties, direct coupling of both compounds was attempted. The reaction was assumed to proceed through Michael addition of nucleophilic sulfhydryl group<sup>2</sup>) followed by concerted aldol condensation.

3-Keto-GA<sub>3</sub> was reacted with ammonium mercaptopyruvate<sup>3)</sup> in ammoniacal solution of pH 8. TLC analysis showed that two major compounds were formed together with more polar compounds. One was found to be gibberethione (20% yield): mp 232~236°C and IR spectrum (3505, 3440, 3330, 1806, 1766, 1709 cm<sup>-1</sup>) were identical with those of authentic specimen. Another compound (54% yield), mp 208~210°C, was an isomer of gibberethione because its methyl ester showed the same molecular ion peak (at m/e 492) as gibberethione dimethyl ester and named isogibberethione. NMR spectrum is as follows;  $\delta$  1.21 (s, CH<sub>3</sub>), 2.74, 4.02 (d, J=9, C6-H and C5-H), 2.93, 3.34 (d, J=12, C3'-H<sub>2</sub>), 3.95, 4.39 (d, J=11, C2-H and C1-H), 4.95, 5.22 (C17-H<sub>2</sub>). The low  $\delta$  values of C2-H and C5-H are suggestive of free C3 ketone. The IR spectrum (3600, 3520, 3430, 3160, 1745, 1713,



1621 cm<sup>-1</sup>) lacked an absorption due to the hindered lactol carbonyl which was observed at 1806 cm<sup>-1</sup> in gibberethione, suggesting that the carboxyl group in the mercaptopyruvic acid moiety is unable to form lactol ring. The bond between C2 and C2' should hold lesshindered  $\beta$ -orientation since NMR experiment showed that the proton at C2 easily exchanged into deuterium in deuteroacetone without any isomerization.<sup>1)</sup> The above data lead to either the structure V or VII. The coupling constant (11 Hz) between C1-H and C2-H favoured the structure VII. However on treatment with 0.1 N of aqueous ammonium hydroxide gibberethione underwent bond-cleavage between C2 and C2' followed by reclosure to yield isogibberethione. This strongly indicates that the structure of isogibberethione is V.

In analogous way 3-keto- $GA_7(II)$  was coupled with mercaptopyruvate to yield IV (named

<sup>\*</sup> The name "gibberethione" is a revised name for "pharbitic acid" since the latter name had been allocated to other compounds.<sup>4)</sup>

gibberethione  $A_7$ ), mp 214~216°C, and VI (semi-crystalline, named isogibberethione  $A_7$ ). The structures were determined in analogy with gibberethione and isogibberethione. The spectral data are as follows. Gibberethione  $A_7$ : IR 3440, 1806, 1767, 1734 cm<sup>-1</sup>; NMR  $\delta$  1.29 (s, CH<sub>3</sub>), 2.72, 3.54 (d, J=10, C6-H and C5-H), 3.05, 4.43 (d, J=8, C2-H and C1-H), 3.18, 3.37 (d, J=12, C3'-H<sub>2</sub>), 4.90, 5.00 (C17-H<sub>2</sub>); MS (dimethyl ester) m/e 476  $(M^+)$ , 288 (base peak). Isogibberethione  $A_7$ : NMR  $\delta$  1.18 (s, CH<sub>3</sub>), 2.77, 4.04 (d, J=9, C6-H and C5-H), 2.95, 3.37 (d, J=12, C3'-H<sub>2</sub>), 3.95, 4.42 (d, J=10, C2-H and C1-H), 4.95, 5.05 (C17-H<sub>2</sub>); MS (dimethyl ester) m/e 476 (M<sup>+</sup>), 288 (base peak).

Microdrop test on dwarf rice Tan-ginbozu seedling revealed that the growth-promoting activity is  $A_3>3$ -keto-GA<sub>3</sub>>gibberethione= isogibberethione (almost inactive);  $GA_7>3$ keto- $GA_7>$  gibberethione  $A_7$ =isogibberethione  $A_7$  (almost inactive). As discussed earlier<sup>1</sup>) formation of gibberethione in plant is possibly concerned in deactivation of  $GA_3$ . Similarly it is possible that deactivation of  $GA_7$  in plant will proceed by formation of gibberethione  $A_7$  via 3-keto- $GA_7$  though such a compound has not yet been found in plant kingdom.

## REFERENCES

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