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SYNTHESIS OF 7-THIOLOGIBBERELLIN A_3 AND A_1 AND THEIR PHOTOCHEMICAL RING CLOSURE TO 7→15α-THIOLOLACTONES[1]

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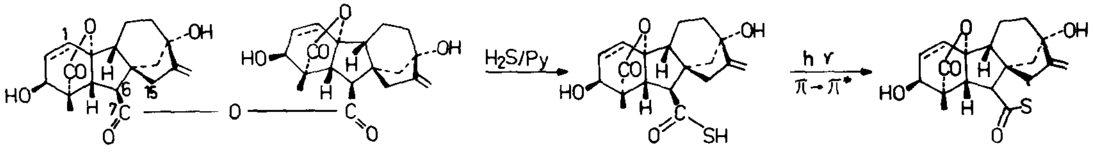
Summary: The thiogibberellin analogs 3 and 4 were synthesized via sulfhydrolysis of the carboxylic acid anhydrides 1 and 2 and transformed photochemically to the corresponding 7→15α-thiololactones 5 and 6.

In contrast to thioesters there are only few reports on the photochemistry of thiocarboxylic acids[2,3]. In continuation of our studies on synthetic photochemistry in the gibberellin series we have prepared the phytohormone thioanalogs 3 and 4 which were transformed in a new photochemical ring closure to the corresponding 7→15α-thiololactones 5 and 6.

Thus, sulfhydrolysis of GA_3 anhydride 1[4] (0.2 mmol) with excess H_2S in 50 ml abs. pyridine (4 h, r.t.) followed by SiO_2 chromatography yielded 56 % 7-thiolo-GA_3 (3) with m.p. 206 °C dec. (ethylacetate/n-hexane) and $[\alpha]_D^{25}$ $+ 54.5^\circ$ (c 0.318, EtOH). MS: M^+ m/z 362.2155 (calc. for $C_{19}H_{22}O_5S$ 362.2093). IR (KBr): ν_{max} 893, 3068 ($>C=CH_2$), 1655 (–CH=CH–), 1720 (COSH), 1760 (γ-lactone), 3440 cm^{-1} (OH). UV (MeOH): λ_{max} (ε) 242 nm (1990). ORD (MeOH): $[M]_{298}$ $+ 5320^\circ$, $[M]_{260}$ $- 10050^\circ$ (a + 154)[5]. 100 MHz ^1H NMR: $\delta_{TMS}^{acetone-d_6}$ 1.25 (s, 18-H_3), 3.33 (d, J = 10 Hz, 6-H), 3.35 (d, J = 10 Hz, 5-H), 4.02 (d, J = 3 Hz, 3-H), 4.91 and 5.23 (m, 17-H_2), 5.90 (dd, J = 9 Hz, J' = 3 Hz, 2-H), 6.40 ppm (d, J = 9 Hz, 1-H). Upon irradiation of 3 (0.3 mmol) in 100 ml ethyl acetate (Hanovia photoreactor, 254 nm, 2 h, r.t., argon) a smooth photoreaction was observed (TLC monitoring) leading after SiO_2 chromatography to 34 % 5 with m.p. 163 °C dec. and $[\alpha]_D^{24}$ $- 126^\circ$ (c 0.3) as the main product. MS: M^+ m/z 360.1032 (calc. for $C_{19}H_{20}O_5S$ 360.1027). IR (nujol): ν_{max} 890 ($>C=CH_2$), 1680 (thiololactone), 1760 (γ-lactone), 3430 cm^{-1} (OH). UV λ_{max} (ε) 241 nm (3150). ORD: $[M]_{300}$ $+ 430^\circ$, $[M]_{250}$ $- 14350^\circ$(a + 148)[5]. The 7→15-thiololactone structure followed from the ^1H-NMR spectrum of 5 with a new one-proton doublet at 4.55 for the 15-H as well as the doublet character (each J = 2 Hz) of the 17-H_2 signals at 4.81 and 5.23 ppm indicating only one allylic coupling. In regard to the stereochemistry at C-15 only 7→15α-connection is possible because of an extreme distortion of the thiolactone ring in the case of a 15ß annelation (Dreiding models). In an analogous



1 Δ¹
2

3 Δ¹
4

5 Δ¹
6

sequence GA$_1$ anhydride 2[6] was transformed via 7-thiolo-GA$_1$(4, 50 %, m.p. 261 °C dec., $[\alpha]_D^{26}$ + 41.1°) to the thiololactone 6 (30 %, m.p. 165 °C dec., $[\alpha]_D^{26}$ + 30.5°) for both also satisfactory physical data were obtained. Thus, $\pi \rightarrow \pi^*$ excitation of the thiocarboxyl chromophore in 3 and 4 results in a regio- and stereoselective ring closure to 7→15α-thiololactones representing to our knowledge the first case of such intramolecular functionalization observed in the photochemistry of thiocarboxylic acids. Further studies on scope and mechanism of this reaction are under way.

Compounds 3 - 6 are further interesting gibberellin analogs modified at the biologically relevant 6-carboxylic function of this phytohormones[7]. In a preliminary bioassay 7-thiolo GA$_3$ (3) showed about 35 % and its thiololactone 5 0.2 % GA$_3$ activity in the dwarf pea test[8].

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