

ANOMALOUS WITTIG REACTION OF ALDONIC THIOAMIDE DERIVATIVES.

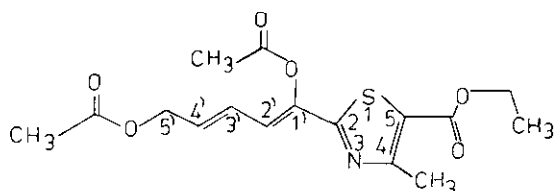
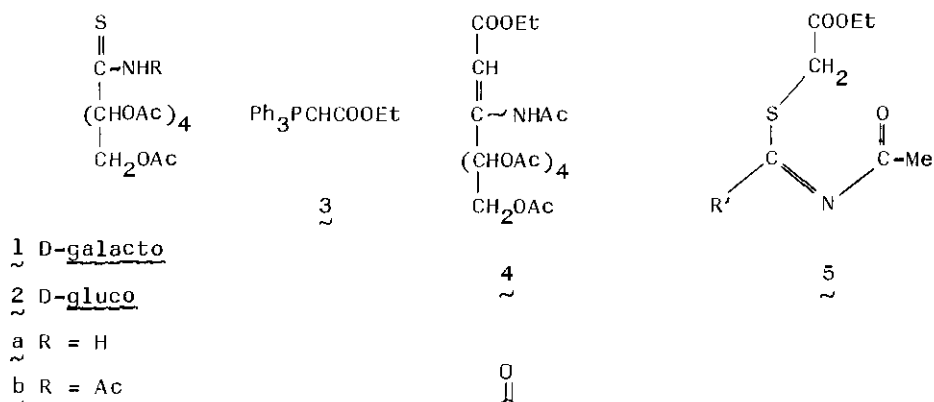
A NEW MODE OF THIAZOLE RING FORMATION

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Abstract - A new mode of thiazole ring formation and an unexpected acetoxy group elimination were observed as a result of the reaction of N-acetyl-per-O-acetylhexonic thioamides (1b and 2b) with ethoxycarbonylmethylenetriphenylphosphorane affording ethyl 2-(1',5'-diacetoxy-penta-1',3'-Z,E-dien-1'-yl)-4-methylthiazole-5-carboxylate (6).

Recently Gossauer et al.¹ described that N-acylthiocarboxamides gave β -acylaminoacrylic acid derivatives with methoxycarbonylmethylenetriphenylphosphorane in a regioselective thiocarbonyl-olefination reaction. As an attempt for the extension of this method to obtain compounds of the type 4 by chain elongation of carbohydrates N-acetyl-per-O-acetyl-D-galactonic thioamide 1b, prepared from 2,3,4,5,6-penta-O-acetyl-D-galactonic thioamide² 1a according to the method of Goerdeler³, was treated with ethoxycarbonylmethylenetriphenylphosphorane 3 in chloroform solution for 12-16 h at 70°C in a sealed tube. After chromatographic separation of the tarry, rather complex reaction mixture only the major component, an optically inactive restrictedly storable compound could be isolated in pure form in an 18% yield. Based on elemental analyses and the molecular ion at m/z 353 a $C_{16}H_{19}NO_6S$ composition was rendered to this compound. Surprisingly, the molecule contained sulphur, no NH band could be detected in the ir-spectrum, and instead of the diffuse OAc carbonyl band of the starting 1b at about ν 1750 cm^{-1} three well-separated bands at ν 1708, 1736 and 1765 cm^{-1} could be assigned. Besides the signals of the ethyl group of the ester function a methyl singlet was detected in the ¹H-nmr spectrum at δ =2.71 ppm, the high chemical

shift of which did not render probable the attribution thereof to either an acetoxy group or to the desired N-acetylenamine function of 4. Of the five expected acetoxy groups only two ones (δ 2.38 and 2.09 ppm) were detected together with three ethylene protons apart the terminal CH_2 group of the sugar-chain. The mass spectrum of the product revealed the fragments m/z 170 and 172 (ethyl methylthiazolecarboxylate $\pm \text{H}$). On this basis an ethyl 2-(diacetoxy-pentadienyl)-methylthiazole-carboxylate structure 6 was suggested.



6

In this reaction, presumably, the active methylene group of the Gossauer's type¹ intermediate N-acetyl-S-alkylthioimide 5 is deprotonated by the basic phosphorane reagent and then condensed into the thiazole derivative⁴. As during the reaction three AcO groups and only one hydrogen atom have departed, the β -elimination of the 2'-AcO and homolytic splitting of the 3'- and 4'-AcO groups must be postulated. In analogous manner N-acetyl-per-O-acetyl-D-gluconic thioamide 2b prepared as above³ from 2a⁵ gave the same product 6 in practically identical yield⁶.

Due to the presence of seven quaternary carbon atoms the ^{13}C -nmr chemical shifts alone did not give satisfactory evidence concerning the supposed structure. To solve the ^{13}C assignment problem the long-range carbon-proton connectivity can be studied by the known one-⁸ and two-dimensional⁹ nmr methods.

However, as the $^2J_{CH}$, $^3J_{CH}$ and $^4J_{CH}$ values showed great differences (cca 1-8 Hz) the 2D DEPT method¹⁰⁻¹² was regarded to be the most efficient. The relatively long 1H and ^{13}C spin-spin relaxation times (ca. 1 sec) allowed the insertion of the theoretical $1/2 \tau = \tau = 0.125$ sec ($\tau = 4$ Hz) interval in the sequence. With this τ parameter all of the important long-range carbon-proton spin-spin couplings could be detected in an overnight experiment on a half mmol of 6. The assignment of the proton-coupled ^{13}C -nmr spectrum allowed the determination of some long-range coupling constants. The value of $^3J_{C-2, H-2'}$ (3.4 Hz¹³) indicates a cis-relationship between C-2 and H-2'. The chemical shifts of carbons C₄, C₅ and 4-CH₃ of 6 are in good agreement with the estimated^a (see Table 1.) values demonstrating the substitution pattern of the thiazole ring of this compound.

Table 1. Characteristic data of 1b, 2b, and 6.

<u>1b</u> ,	mp 140-142°C
<u>2b</u> ,	mp 116-118°C
<u>6</u>	mp 78-79°C; 1H -nmr (200 MHz, CDCl ₃ , TMS, first order analysis): δ (ppm) 1.33 (t, 3 H, CH ₃ (Et)), 2.09 (s, 3 H, OAc (5')), 2.38 (s, 3 H, OAc (1')), 2.71 (s, 3 H, CH ₃ (4)), 4.33 (q, 2 H, CH ₂ (Et)), 4.67 (m, 2 H, H-5'a, H-5'b), 6.13 (dt, 1 H, H-4'), 6.38 (ddt, 1 H, H-3'), 7.05 (dd, 1 H, H-2'); $^3J_{2',3'} = 11.0$ Hz, $^4J_{2',4'} \approx 0.5$ Hz, $^3J_{3',4'} = 15.2$ Hz, $^4J_{3',5'a} \approx 1.2$ Hz, $^4J_{3',5'b} \approx 1.2$ Hz, $^3J_{4',5'a} = 6$ Hz, $^3J_{4',5'b} = 6$ Hz; ^{13}C -nmr (50 MHz, CDCl ₃ , TMS): δ (ppm) 14.05 (CH ₃ (Et)), 17.25 (CH ₃ (4) (16.2 ^a)), 20.14 (CH ₃ (1'-OAc)), 20.50 (CH ₃ (5'-OAc)), 61.04 (CH ₂ (Et)), 63.91 (C-5'), 120.11 (C-2'), 122.12 (C-5, (123.6 ^a)), 125.15 (C-3'), 133.32 (C-4'), 140.36 (C-1'), 161.03 (C-4, (157 ^a)), 161.61 (C=O (OEt)), 164.28 (C-2), 167.77 (C=O (1'-OAc)), 170.08 (C=O (5'-OAc)).

^a Expected chemical shifts based on a substructure search.

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