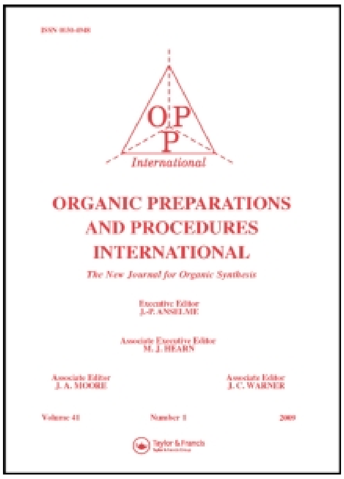

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SUGAR 1,3,4-OXADIAZOLES. IV: THE SYNTHESIS OF SUGAR 1,3,4-OXADIAZOLINE DERIVATIVES

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SUGAR 1,3,4-OXADIAZOLES. IV[1]: THE SYNTHESIS OF SUGAR 1,3,4-OXADIAZOLINE DERIVATIVES[2]

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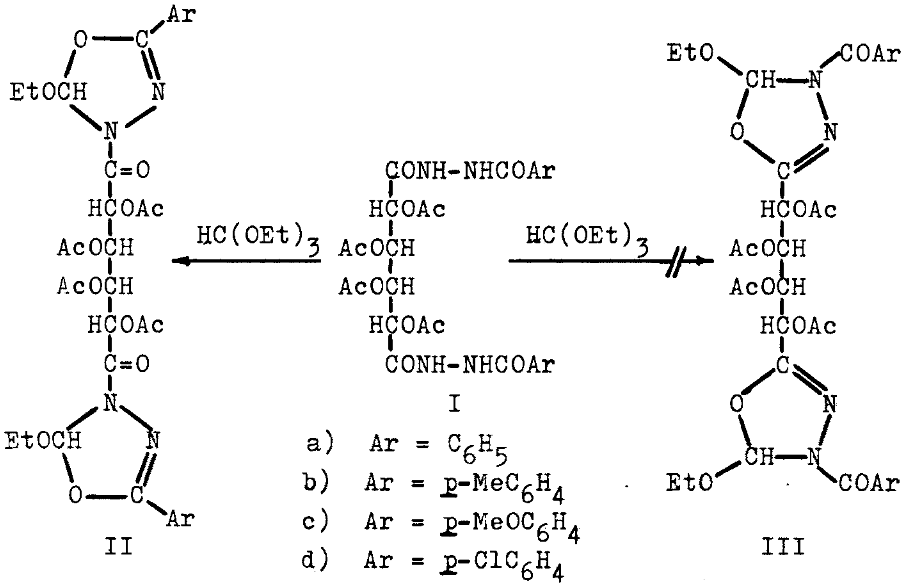
This paper reports the synthesis of sugar bis(Δ^2-1,3,4-oxadiazoline) derivatives II[1,2] by condensative cyclization[3]. Thus, condensative cyclization of 2,3,4,5-tetra-O-acetyl-galactaric acid bis(aroylhydrazides) (I)[1] was effected by heating with triethyl orthoformate in dioxane to give optically inactive products.



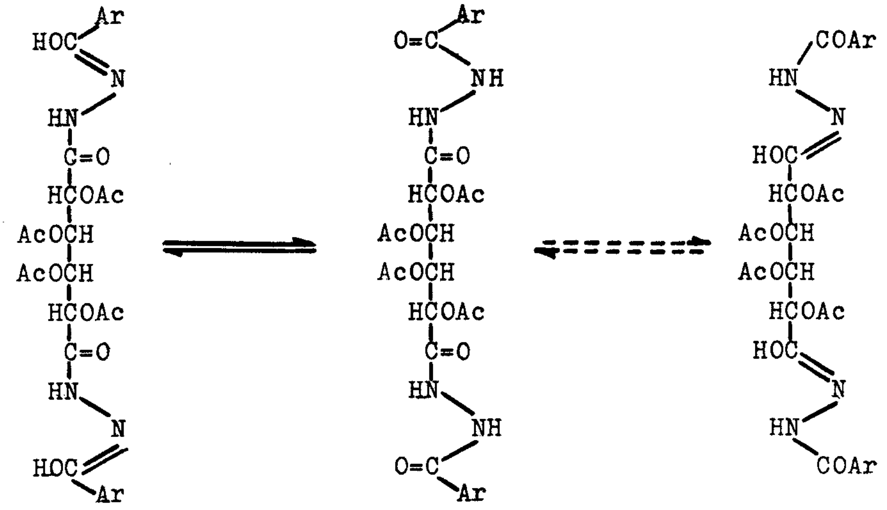
II

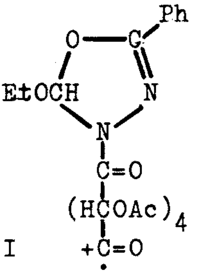
I

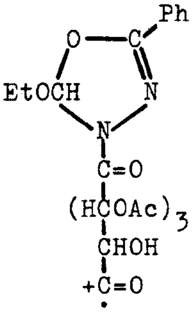
a) Ar = C_6H_5
b) Ar = p-MeC_6H_4
c) Ar = p-$MeOC_6H_4$
d) Ar = p-ClC_6H_4

III

IR and NMR (see experimental) were in agreement with both structures II and III arising from the condensative cyclization of triethyl orthoformate with either of the two possible enolic forms of I (IV and V) and could not distinguish between them. However, the mass spectrum of the cyclization product from Ia showed in addition to a molecular ion peak at m/e 726, fragments VI and VII at m/e 535 and 493 respectively.




VI


VII

These two fragments would only be expected from structure II. Accordingly, the cyclization products were assigned the structure of 2,3,4,5-tetra-*O*-acetylgalactaroyl-1,6-bis(5-aryl-2-ethoxy-2,3-dihydro-1,3,4-oxadiazol-3-yl) (II). This assignment implies that, under the reaction conditions used, the enolic structure IV is the preponderant (or sole) existing entity and this is compatible with the fact that the aroylhydrazido groups of I should be more enolizable than the tetra-O-acetylgalactaroylhydrazido groups, due to the greater electron-withdrawing effect of the polyacetoxyalkyl chain as compared to that of the phenyl groups.

EXPERIMENTAL

Melting points were determined with a Kofler block and are uncorrected. The IR spectra were recorded on a Unicam SP200 spectrophotometer. The NMR spectra were determined at 60 MHz with a Varian T-60 spectrometer for solutions in $CDCl_3$ containing 1% tetramethylsilane as the internal standard. The mass spectra were performed on a Hitachi-Perkin-Elmer RMU-6 mass spectrometer. Microanalyses were determined in the Microanalyses Unit, Faculty of Science, Cairo University, Cairo, Egypt. Homogeneity of the products were checked by TLC on Silica Gel G plates (layer thickness 0.25 mm) and the spots were detected with iodine or by spraying with 20% sulfuric acid (v/v) followed by heating the chromatograms on a hot plate for a few minutes.

2,3,4,5-Tetra-O-acetylgalactaroyl-1,6-bis(5-aryl-2-ethoxy-2,3-dihydro-1,3,4-oxadiazol-3-yl) (II).— To a suspension of 2,3,4,5-tetra-O-acetylgalactaroyl bis(aroylhydrazides)[1](I, 2 mmoles) in dioxane (10 ml), triethyl orthoformate (5 mmoles) was added and the mixture was heated under reflux until complete dissolution occurred (20-30 hrs). The mixture was evaporated to dryness and the residue crystallized from ethanol.

The IR spectra of the cyclization products showed absorptions at 1740-1760 (OAc), 1690-1705 (CON), 1630-1635 (C=N), 1070 (C-O-C), 970-1035 (C-O), and 770-680 cm^{-1} (Ph). The spectra lacked the NH and CONH absorptions of the parent bishydrazides. The NMR spectrum of the cyclization product from Ia showed signals of two methyl groups at δ 1.25 as 6-proton triplet (J=3.5 Hz), four O-acetyl groups as two 6-proton singlets at δ 2.13 (2 Ac) and 1.95 (2 Ac), two methylene groups at δ 3.76 as 4-proton quadruplet (J=3.5 Hz), 2-proton singlet at δ 6.93 due to H-2 of the two heterocyclic rings, and two phenyl groups as 10-proton multiplet at δ 7.80-7.40. the rest of the sugar chain protons appeared between δ 6.40-5.70.

TABLE 1. 2,3,4,5-Tetra-O-acetylgalactaroyl-1,6-bis(5-aryl-2-ethoxy-2,3-dihydro-1,3,4-oxadiazol-3-yl) (IIa-IId)

Cpd No.	Yield %	Mp. °C	Formula	Anal. $\frac{\text{Found}}{\text{Calcd}}$ C	H	N
IIa	78	189-191	$C_{34}H_{38}N_4O_{14}$	$\frac{56.7}{56.2}$	$\frac{5.7}{5.3}$	$\frac{7.6}{7.7}$
IIb	81	269-270	$C_{36}H_{42}N_4O_{14}$	$\frac{57.3}{57.3}$	$\frac{5.4}{5.6}$	$\frac{7.5}{7.4}$
IIc	76	254-256	$C_{36}H_{42}N_4O_{16}$	$\frac{55.0}{55.0}$	$\frac{5.0}{5.4}$	$\frac{7.1}{7.1}$
IId	83	260-262	$C_{34}H_{38}N_4Cl_2O_{14}$	$\frac{51.1}{51.2}$	$\frac{4.6}{4.8}$	$\frac{7.3}{7.0}$

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