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Preliminary communication

1,3,4-Oxadiazolines *via* acetylation of D-galactose acylhydrazones

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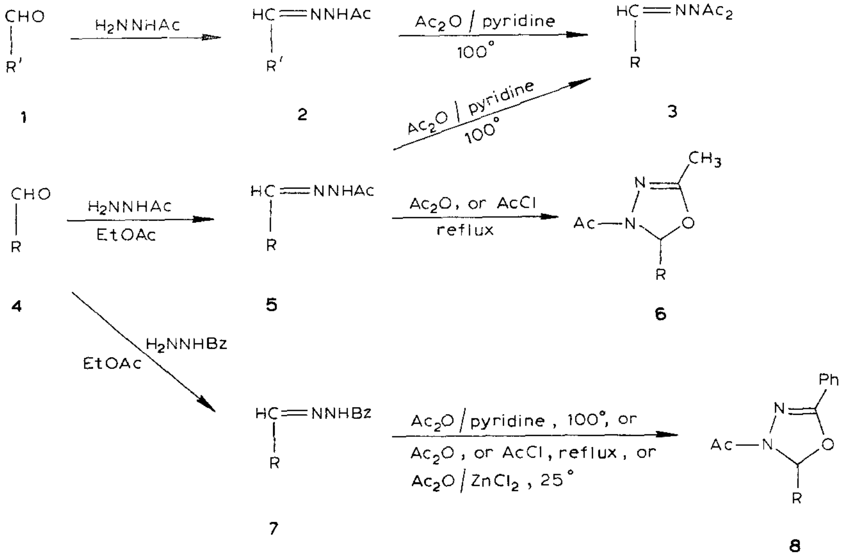
El Khadem and his co-workers[1] reported that acetylation of penta-*O*-acetyl-*aldehydo*-D-galactose acetylhydrazone (5) [m.p. 190° (from ethanol–water), ν_{max}^{KBr} 1690 cm^{-1} (CONH), obtained from *aldehydo*-D-galactose acetylhydrazone (2) by treatment with acetic anhydride in pyridine at room temperature] with boiling acetic anhydride gave penta-*O*-acetyl-*aldehydo*-D-galactose *N,N*-diacetylhydrazone (3), m.p. 256° (from ethanol–water), ν_{max}^{KBr} 1670 cm^{-1} (CONCO). Similarly, penta-*O*-acetyl-*aldehydo*-D-galactose benzoylhydrazone (7) was reported to give penta-*O*-acetyl-*aldehydo*-D-galactose *N*-acetyl-*N*-benzoylhydrazone, m.p. 124° (from ethanol–water), ν_{max}^{KBr} 1680 cm^{-1} (CONCO).

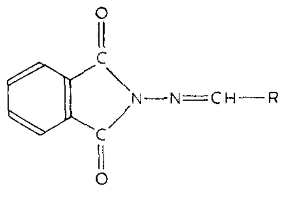
We considered the above ν_{max} values of *N,N*-diacylhydrazones to be unusually low; also, ν_{max} for the amide band of the *N,N*-diacetylhydrazone was shifted downfield by 20 cm^{-1} compared to the corresponding band of the starting acetylhydrazone.

Penta-*O*-acetyl-*aldehydo*-D-galactose *N,N*-diacetylhydrazone (3) was first prepared by Helferich and Schirp[2] by treatment of D-galactose acetylhydrazone (2) with acetic anhydride in pyridine at 100°, and was reported to have m.p. 193–194° (from propan-2-ol), $[\alpha]_D^{21}$ +53.3° (chloroform).

In order to elucidate the above-mentioned discrepancies in the physical constants of 3, the acetylation of 2, 5, and 7 was reinvestigated using acetyl chloride and acetic anhydride in the presence of basic and acidic catalysts. Treatment of 2 and 5 {m.p. 200° (from ethanol–water), $[\alpha]_D^{23}$ +50.5° (*c* 1, chloroform); ν_{max}^{KBr} 1687 and 1681sh cm^{-1} (CONH); p.m.r. data (100 MHz, chloroform-*d*): δ 6.94 (d, 1 H, *J* ~4 Hz, C*H*=N), prepared from penta-*O*-acetyl-*aldehydo*-D-galactose (4) and acetylhydrazine in boiling ethyl acetate} with acetic anhydride–pyridine at 100° gave the same product, the physical data {m.p. 193–195° (from chloroform–heptane), $[\alpha]_D^{23}$ +47.5° (*c* 1, chloroform)} of which are in good agreement with those of 3 reported by Helferich and Schirp[2]. The structure penta-*O*-acetyl-*aldehydo*-D-galactose *N,N*-diacetylhydrazone for this compound was supported by the value (1710 cm^{-1}) of the CO–N–CO i.r.-band, as well as by the p.m.r. signals at δ 7.74 (d, 1 H, *J* ~3 Hz, C*H*–N) and 2.0–2.32 (7 Ac).

The crude product obtained from 5 by treatment with boiling acetic anhydride[1]





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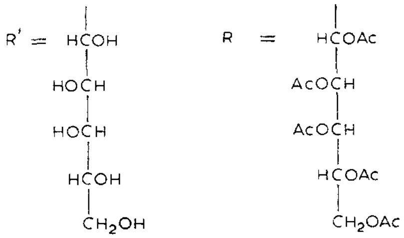

(or boiling acetyl chloride) had m.p. 215° (shrinking at 187°), $[\alpha]_D^{23}$ $-150°$ (*c* 1, chloroform). The high $[\alpha]_D$ value was not consistent with the proposed[1] diacetylhydrazone structure. The crude product was a mixture of diastereoisomers, and its p.m.r. spectrum contained signals at δ 6.20 (s) and 5.97 (d, J ~6 Hz) for $\mathrm{R{-}\underset{\displaystyle N}{\underset{|}{C}}\mathit{H}{-}O}$. Crystallisation from ethyl acetate gave a pure product {m.p. 216–217°, $[\alpha]_D^{23}$ $-186°$ (*c* 1, chloroform); ν_{max}^{KBr} 1667 cm^{-1} (CON); δ 6.20 (s, 1 H, $\mathrm{O{-}\underset{\displaystyle N}{\underset{|}{C}}\mathit{H}{-}R}$) and 2.0–2.12 (7 Me)} which was assigned the structure 3-acetyl-5-methyl-2-(D-*galacto*-1,2,3,4,5-penta-acetoxypentyl)-1,3,4-oxadiazoline (**6**).

Likewise, treatment of **7**[3] [m.p. 192° (from ethyl acetate); ν_{max}^{KBr} 1658 cm^{-1} (CONH); δ 7.3–7.8 (6 H, 5 aromatic and 1 C*H*=N), 9.5 (s, 1 H, CON*H*), and 2.0–2.1 (5 Ac)] with boiling acetic anhydride or acetyl chloride, or acetic anhydride–zinc chloride at room temperature, gave a mixture of diastereoisomeric 3-acetyl-2-(D-*galacto*-1,2,3,4,5-penta-acetoxypentyl)-5-phenyl-1,3,4-oxadiazolines (**8**) and not the *N*-acetyl-*N*-benzoylhydrazone.

The conversion **7**→**8** was also effected with hot acetic anhydride–pyridine. The proportions of the diastereoisomers depended on the nature of the catalyst (basic or acidic). Fractional crystallisation of the mixture of diastereoisomers from ethyl acetate and ethyl acetate–heptane gave (–)-**8**, m.p. 148°, $[\alpha]_D^{23}$ –209° (*c* 1, chloroform); ν_{max}^{KBr} 1679 and 1653sh cm^{-1} (CON); δ 6.38 (s, 1 H, O–C*H*–R) and 1.9–2.02 (6 Ac); and (+)-**8**. m.p. 130°,

N

$[\alpha]_D^{23}$ +230° (*c* 1, chloroform); ν_{max}^{KBr} 1678, 1653 (CON), and 1640 cm^{-1} (C=N); δ 6.20 (d, 1 H, *J* ~ 6 Hz, O–C*H*–R) and 2.0–2.25 (6 Ac).

N

For the purpose of spectroscopic studies, penta-*O*-acetyl-*aldehydo*-D-galactose phthaloylhydrazone {**9**, m.p. 183° (from ethanol), $[\alpha]_D^{23}$ –28° (*c* 1, chloroform); ν_{max}^{KBr} 1790 and 1730 cm^{-1} (CONCO); δ 8.40 (d, 1 H, *J* ~4 Hz, C*H*–N) and 1.98–2.14 (5 Ac)}, which has the *N,N*-diacyl structure, was prepared from **4** and *N*-aminophthalimide.

Thus, the compounds reported by El Khadem *et al.*[1] are 1,3,4-oxadiazoline derivatives and not *N,N*-diacylhydrazones.

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