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Note

Synthesis of some saccharide hydrazones having *p*-aminobenzoic acid and *p*-aminosalicylic acid moieties, and their reactions*

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p-Aminobenzoic acid (PABA), a member of the vitamin B complex, is involved in the synthesis of folic acid coenzymes and pteroylglutamic acid (a compound having full folic acid activity)[2]; such coenzymes are essential growth-factors for some micro-organisms[3], as well as in the conversion of certain precursors into purines[4]. PABA is used as an antirickettsial agent[5]. The corresponding 2-hydroxy derivative, *p*-aminosalicylic acid (PAS), aids streptomycin and dihydrostreptomycin in the treatment of tuberculosis[6]. Structural modifications of PAS showed that the maximum activity is achieved by this particular substitution. However, esters, hydrazides, and acylamino derivatives, which are labile enough to be hydrolyzed *in vivo* to PAS, are sometimes preferred, because they cause less gastric irritation[7]. In connection with these aspects, as well as our studies on the synthesis and reactions of hydrazone derivatives[8–19] in the carbohydrate series, we have synthesized some saccharide hydrazones having the PABA and PAS fragments, and have studied their reactions. Thus, condensation of equimolar equivalents of a monosaccharide and (*p*-acetamidobenzoyl)hydrazine or (*p*-acetamidosalicoyl)hydrazine in ethanolic solution afforded the corresponding hydrazone. D-Galactose, D-mannose, D-arabinose, D-xylose, and lactose (*p*-acetamidobenzoyl)hydrazones (**1–5**), and D-galactose and lactose (*p*-acetamidosalicoyl)hydrazones (**6** and **7**) were prepared in this way. Acetylation of **1–3** with acetic anhydride in pyridine afforded the corresponding per-*O*-acetyl derivatives (**8–10**). The infrared (i.r.) spectra of the acetates showed, in addition to the OCN bands that also appeared in the spectra of their precursors, an acetyl band at 1735–1730 cm^{-1}. On the other hand, treatment of **8** with boiling acetic anhydride caused its cyclization, giving the corresponding oxadiazoline formulated as 5-(*p*-acetamidophenyl)-3-acetyl-2-(penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1,3,4-

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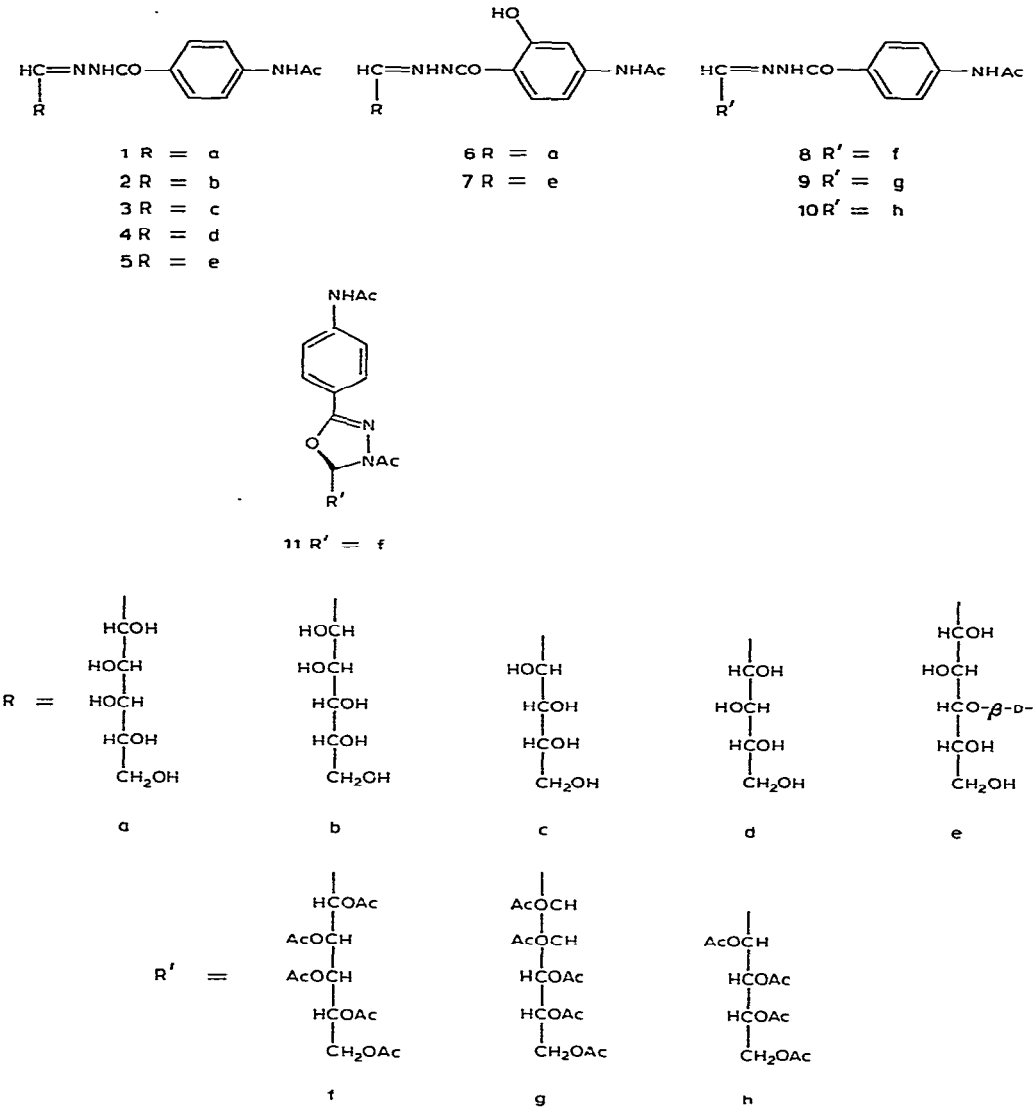

oxa-diazoline (**11**), similar to the structure given[18,19] for the products obtained from similar reactions.

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler-block apparatus and are uncorrected. I.r. spectra were recorded with a Beckman IR-4210 spectrophotometer. Microanalyses were performed in the Chemistry Department, Faculty of Science, Cairo University, Cairo, Egypt.

TABLE I

MICROANALYTICAL AND SPECTRAL DATA FOR SUGAR HYDRAZONES (1–7)

Compound	R	Yield (%)	M.p. (degrees)	Molecular formula	Calculated (%)			Found (%)			ν_{max}^{Nujol} (cm^{-1})
					C	H	N	C	H	N	
1	a	80	215–216	$C_{15}H_{21}N_3O_7$	50.7	6.0	11.8	50.7	6.2	11.5	1640
2	b	71	201–202	$C_{15}H_{21}N_3O_7$	50.7	6.0	11.8	50.9	6.3		1637
3	c	77	219–220	$C_{14}H_{19}N_3O_6$	51.7	5.8	12.9	51.4	5.8	12.7	1660, 1630
4	d	69	176–180	$C_{14}H_{19}N_3O_6$	51.7	5.8	12.9	51.6	5.5	12.6	1655, 1620
5	e	75	212–213	$C_{21}H_{31}N_3O_{12}$	48.7	5.9	8.1	48.5	5.7	8.4	1660
6	a	82	184–185	$C_{15}H_{22}N_3O_8$	48.4	5.9	11.3	48.6	5.8	11.1	1630
7	e	74	212–214	$C_{21}H_{31}N_3O_{13}$	47.3	5.8	7.9	47.6	6.1	7.6	1625

TABLE II

MICROANALYTICAL AND SPECTRAL DATA FOR THE ACETYL DERIVATIVES OF SUGAR (*p*-ACETAMIDOBENZOYL)-HYDRAZONES (8–10) AND THEIR REACTION PRODUCT (11)

Compound No	R	Yield (%)	M.p. (degrees)	Molecular formula	Calculated (%)			Found (%)			ν_{max}^{Nujol} (cm^{-1})
					C	H	N	C	H	N	
8	f	66	205–206	$C_{25}H_{31}N_3O_{12}$	53.1	5.4	7.4	53.4	5.7	7.6	1730, 1670(sh), 1650
9	g	65	167–169	$C_{25}H_{31}N_3O_{12}$	53.1	5.4	7.4	52.9	5.1	7.7	1730, 1650
10	h	75	218–219	$C_{22}H_{27}N_3O_{10}$	53.5	5.5	8.5	53.3	5.6	8.7	1735, 1667, 1640
11	f	72	152–153	$C_{27}H_{33}N_3O_{13}$	53.4	5.4	6.9	53.2	5.5	6.8	1745, 1695, 1635

Saccharide (p-*acetamidobenzoyl*)*hydrazones* (**1–5**). — A solution of the sugar (0.01 mol) in water (4 mL) was treated with (*p*-acetamidobenzoyl)hydrazine (0.01 mol) in ethanol (300 mL), and the mixture was boiled under reflux for 1 h. The resulting solution was concentrated, and the concentrate cooled, whereupon the product separated out. It was filtered off, washed with ethanol, dried, and recrystallized from ethanol, giving colorless needles (see Table I).

Saccharide (p-*acetamidosalicoyl*)*hydrazones* (**6** *and* **7**). — When a solution of the sugar (0.01 mol) in water (4 mL) was treated with (*p*-acetamidosalicoyl)hydrazine (0.01 mol), and the reaction mixture was processed as just described, the corresponding hydrazones separated out; these were recrystallized from ethanol (see Table I).

Poly-O-*acetyl*-aldehydo-*saccharide* (p-*acetamidobenzoyl*)*hydrazones* (**8–10**). —

A solution of the hydrazone (2 g) in a mixture of *N,N*-dimethylformamide (20 mL) and dry pyridine (15 mL) was treated with acetic anhydride (16 mL), and the mixture was kept overnight at room temperature. The mixture was poured onto crushed ice, and the product that separated out was filtered off, washed successively with water and sodium hydrogencarbonate solution, and dried. The products were recrystallized from ethanol, giving colorless needles (see Table II).

*5-(*p*-Acetamidophenyl)-3-acetyl-2-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)-1,3,4-oxadiazoline* (**11**). — A suspension of compound **8** (1 g) in acetic anhydride (10 mL) was boiled under reflux for 2 h, cooled, and poured onto crushed ice. The product was recrystallized from ethanol, giving colorless needles (see Table II).

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