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Note

Reactions of 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoylhydrazine

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This report continues our work on the synthesis of heterocyclic compounds from saccharide derivatives[1–7]. Recently, 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoylhydrazine was condensed[6] with a series of aldehydes to give the corresponding *N*′-arylidene-*N*-[2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoyl]hydrazones (**1–4**). We have now cyclized these compounds with acetic anhydride to 3-(4-acetyl-5-aryl-1,3,4,-oxadiazolin-2-yl)-2-methyl-5-(D-*arabino*-tetraacetoxybutyl)furans (**5–8**), which could be isolated in yields ranging from 20 to 38% (Scheme 1). The structure of these oxadiazoline derivatives was established by their forming *O*-deacetylated products **9–12** when treated with either 3% NaOMe or NH_4OH. The structures were also confirmed by IR and ^{1}H NMR spectroscopy, wherein the C=N, NAc, and OAc bands appeared at the expected frequencies, and all protons showed appropriate resonances in their ^{1}H NMR spectra (for details, see Table I and the Experimental section).

Periodate oxidation of hydrazone **4** afforded the corresponding formyl derivative[6] **13**, which condensed with a number of aroylhydrazines to furnish the corresponding new aroylhydrazones **14–19** (Scheme 1). As expected, the IR spectra showed the disappearance of the aldehydic band (for details, see the Experimental section and Table I). *N*-[5-Formyl-(*p*-toluoylhydrazone)-2-methyl-3-furoyl]cinnamaldehyde-hydrazone (**15**) underwent cyclization with iodine and yellow mercuric oxide in the presence of magnesium oxide at room temperature to afford 2-methyl-3-[5-styryl-(1,3,4-oxadiazol-2-yl)]-5-[5-(*p*-tolyl)-(1,3,4-oxadiazol-2-yl)]furan (**20**) (Scheme 1). The IR spectrum revealed the disappearance of both the NH and CO bands (for details, see the Experimental section).

EXPERIMENTAL

General methods.—Melting points were determined on a Kofler block and are uncorrected. IR spectra were recorded on Unicam SP 1025 and SP 2000 spectrophotometers. ^{1}H NMR spectra were recorded with a Varian EM-90 instrument

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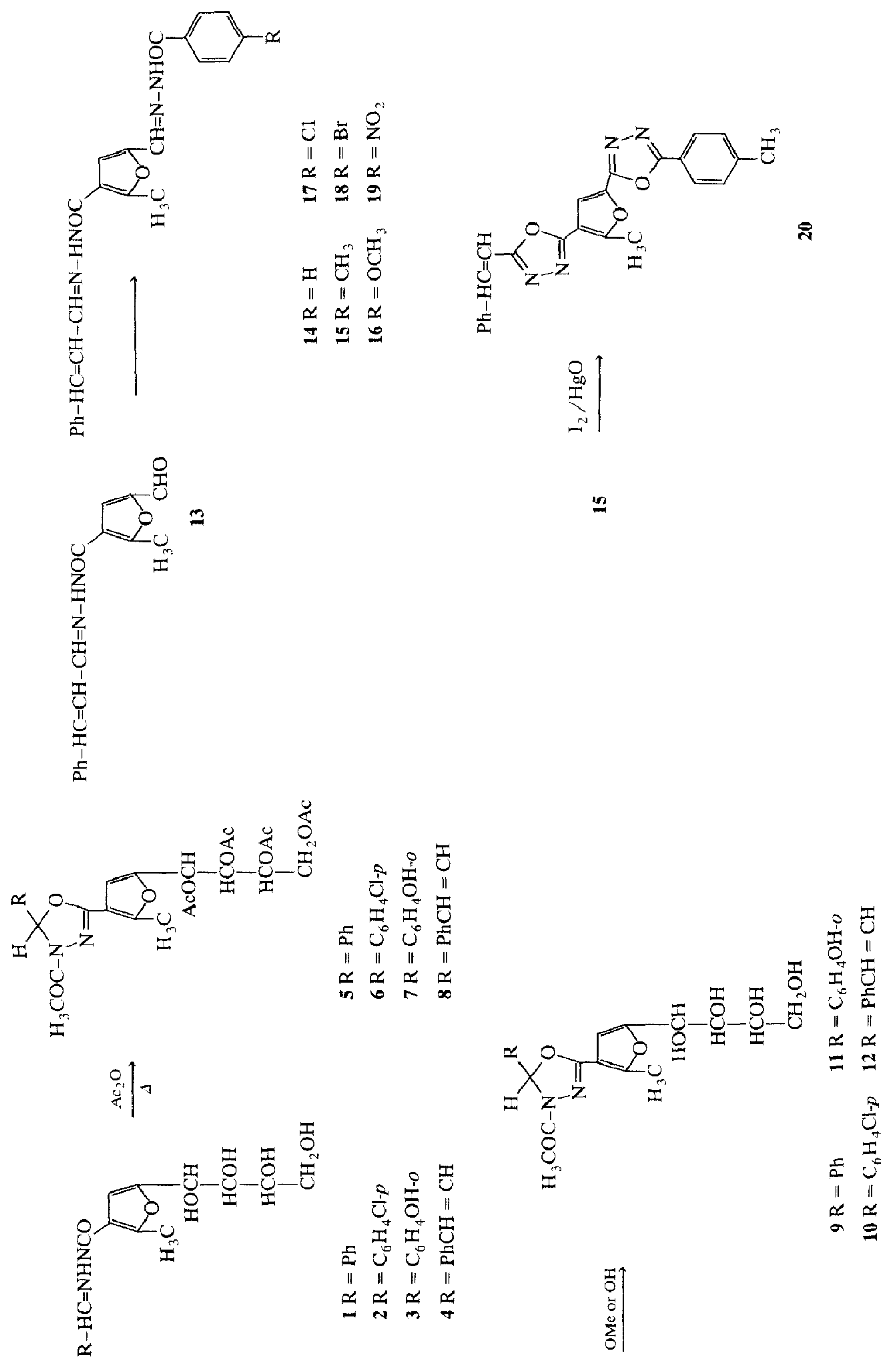
R–HC=NHNCO
H3C
HOCH
HCOH
HCOH
CH2OH
1 R = Ph
2 R = C6H4Cl-p
3 R = C6H4OH-o
4 R = PhCH = CH
Ac2O
Δ
H3COC–N
H
R
O
N
H3C
AcOCH
HCOAc
HCOAc
CH2OAc
5 R = Ph
6 R = C6H4Cl-p
7 R = C6H4OH-o
8 R = PhCH = CH
OMe or OH
H3COC–N
HOCH
HCOH
HCOH
CH2OH
9 R = Ph
10 R = C6H4Cl-p
11 R = C6H4OH-o
12 R = PhCH = CH
Ph–HC=CH–CH=N–HNOC
CHO
13
Ph–HC=CH–CH=N–HNOC
CH=N–NHOC
14 R = H
15 R = CH3
16 R = OCH3
17 R = Cl
18 R = Br
19 R = NO2
15
I2 /HgO
Ph–HC=CH
N–N
CH3
20

TABLE I

Analytical data for compounds **5–20**

Compound no.	MP (°C)	Yield (%)	Molecular formula	Anal. Calcd/Found		
				C	H	N
5	Syrup	20	$C_{27}H_{30}N_2O_{11}$	58.06	5.38	5.02
				58.10	5.34	5.30
6	158	32	$C_{27}H_{29}ClN_2O_{11}$	54.67	4.89	4.72
				54.89	5.01	4.54
7	Syrup	27	$C_{27}H_{30}N_2O_{12}$	56.44	5.23	4.88
				56.23	5.51	5.20
8	Syrup	38	$C_{29}H_{32}N_2O_{11}$	59.59	5.48	4.79
				59.37	5.78	5.03
9	150	17	$C_{19}H_{22}N_2O_7$	58.46	5.64	7.18
				58.68	5.71	7.49
10	130	28	$C_{19}H_{21}ClN_2O_7$	53.71	4.95	6.59
				53.56	5.21	6.87
11	215	28	$C_{19}H_{22}N_2O_8$	56.16	5.42	6.89
				56.01	5.24	7.11
12	Syrup	14	$C_{21}H_{24}N_2O_7$	60.58	5.77	6.73
				60.89	6.08	6.88
14[6]	200	26	$C_{23}H_{20}N_4O_3$	69.01	5.03	14.01
				69.34	4.92	13.85
15	205	68	$C_{24}H_{22}N_4O_3$	69.57	5.31	13.53
				69.30	5.62	13.25
16	204	33	$C_{24}H_{22}N_4O_4$	66.98	5.12	13.02
				66.65	5.41	13.27
17	208	17	$C_{23}H_{19}ClN_4O_3$	63.52	4.37	12.89
				63.22	4.59	13.01
18	220	53	$C_{23}H_{19}BrN_4O_3$	57.62	3.97	11.69
				57.54	3.72	11.81
19	210	57	$C_{23}H_{19}N_5O_5$	62.02	4.27	15.73
				62.27	4.59	15.99
20	195	13	$C_{24}H_{18}N_4O_3$	70.24	4.39	13.66
				70.03	4.68	13.99

with Me_4Si as the internal standard. Mass spectra were obtained from a Nuchik 12-90-G Instrument. Microanalyses were performed at the Faculty of Science, Cairo University, Cairo, Egypt. Solutions were evaporated under diminished pressure unless otherwise stated.

*3-(4-Acetyl-5-aryl-1,3,4-oxadiazolin-2-yl-2-methyl-5-(*D-arabino*-tetraacetoxybutyl)-furans* (**5–8**).—Arylidene hydrazones **1–4** (1.0 g) were each boiled with Ac_2O (15 mL) for 1 h, and the mixture was then poured onto crushed ice (200 g), whereby the title compound was isolated, washed thoroughly with H_2O, and dried. The residue was purified by column chromatography (silica gel) eluted with 20:1 (v/v) EtOAc–hexane; IR 1590–1610 (C=N), 1640–1670 (NAc), and 1740 cm^{-1} (OAc); ^1H NMR (acetone-d_6) for **4**: δ 1.9 (s, 3 H, CH_3 at C-2), 1.95–2.05 (m, 12 H, 4 OAc), 2.5 (s, 3 H, NAc), 5.0–5.9 (m, 5 H, sugar part), 6.4 (s, 1 H, furan C-4), 6.75 (d, 2 H, CH=CH), 7.3–7.5 (m, 5 H, Ar-H), and 7.65 ppm (s, 1 H, oxadiazoline).

*3-(4-Acetyl-5-aryl-1,3,4-oxadiazolin-2-yl)-2-methyl-5-(5-*D-arabino-*tetrahydroxybutyl)furans* (**9–12**).—*Method A.* A solution of the appropriate acetyl derivative of **5–8** in 3% NaOMe in MeOH (10 mL) was kept overnight at room temperature. Amberlite IR-120 (H^+) resin (5 g) was added until the solution was neutral, whereby the oxadiazoline derivative separated. The product was filtered, washed with EtOH and dried.

Method B. To a solution of the appropriate acetyl derivative of **5–8** in MeOH (5 mL), ammonia solution (10%, 3 mL) was added with stirring overnight. The oxadiazoline derivative that separated was filtered, washed with EtOH, and dried. IR: 1590–1600 (C=N), 1640–1680 (NAc), and 3300–3440 cm^{-1} (OH); ^1H NMR (acetone-d_6) for **10**: δ 2.2 (3 H, s, CH_3), 2.23 (3 H, s, $NCOCH_3$), 2.35–3.95 (9 H, m, sugar part), 7.2 (1 H, s, CH-furan), 7.5–7.7 (4 H, m, Ar-H), and 7.9 ppm (1 H, s, CH); CI CIMS: [m/z(%)]: M^+ 424(6.66), 406(5.33), 333(17.33), 291(40), 229(29.33), 211(82.66), 151(45.33), 137(44), and 43(100).

N-*[5-Aroylhydrazonomethyl-2-methyl-3-furoyl]cinnamaldehyde hydrazones* (**14–19**).—To a solution of **13** (1 mmol) in EtOH (10 mL) containing HOAc (0.01 mL) the benzoylhydrazine or its derivative (1 mmol) in EtOH (5 mL) was added. The mixture was heated under reflux for 1 h, whereby the hydrazone derivative separated upon cooling. The product was filtered, washed with EtOH (5 mL), and crystallized from 1:1 $CHCl_3$–EtOH; IR: 1590–1610 (C=N), 1640–1650 (CONH), and 3180–3260 cm^{-1} (NH).

*2-Methyl-3-[5-styryl-(1,3,4-oxadiazol-2-yl)]-5-[5-(*p-*tolyl)-(1,3,4-oxadiazol-2-yl)]-furan* (**20**).—A solution of **15** (0.8 g) in dry Et_2O (50 mL) was stirred with yellow HgO (1.5 g), MgO (0.15 g), and I_2 (1.5 g) for 48 h at room temperature under anhydrous conditions. The solids were filtered off and the Et_2O layer washed with KI solution, $Na_2S_2O_3$, and H_2O, respectively, and dried over anhyd Na_2SO_4. Evaporation of the Et_2O gave a yellow syrup which crystallized from EtOH as needles. An additional crop was obtained by extracting the inorganic residue with hot $CHCl_3$, which upon concentration and dilution with petroleum ether yielded the same product; IR: 1610 (C=N) and 3000 cm^{-1} (CH).

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