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CARBOHYDRATE
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Note

Synthesis and reactions of 5-(D-*arabino*-tetrahydroxybutyl)-3-(2,3-dihydro-1,3,4-oxadiazole-2-thion-5-yl)-2-methylfuran and 5-(D-*arabino*-tetrahydroxybutyl)-3-(2-substituted amino-1,3,4-oxadiazol-5-yl)-2-methylfuran

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In continuation of our work on the synthesis of nitrogen heterocycles from saccharide derivatives [1–7], 5-(D-*arabino*-tetrahydroxybutyl)-3-(2,3-dihydro-1,3,4-oxadiazole-2-thion-5-yl)-2-methylfuran (**2**) was prepared when 5-(D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoylhydrazine [4] (**1**) was allowed to react with carbon disulfide in hot ethanolic potassium hydroxide solution [8,9]. The structure of **2** was confirmed by IR, ^{1}H NMR, and MS spectroscopy (see Experimental).

Reaction of **2** with a number of aromatic amines afforded the corresponding Mannich bases 5-(D-*arabino*-tetrahydroxybutyl)-3-(2,3-dihydro-3-(arylaminomethyl)-1,3,4-oxadiazole-2-thion-5-yl)-2-methylfuran (**3**–**6**) in high to moderate yields (see Scheme 1 and Table 1). Oxidation of **2** with hydrogen peroxide in acetic acid gave the corresponding 2-oxo-oxadiazole derivative **7**, while periodate oxidation afforded the 5-formyl derivative **8**.

When the hydrazide **1** was condensed with allyl- or phenyl-isothiocyanate, it afforded the corresponding 1-(5-D-*arabino*-tetrahydroxybutyl)-2-methylfuro-3-yl)-4-substituted thiosemicarbazides (**9** and **10**, respectively), which were easily cyclodesulfurized with yellow mercuric oxide to afford 5-(D-*arabino*-tetrahydroxybutyl)-3-(2-substituted amino-1,3,4-oxadiazol-5-yl)-2-methylfurans **11** and **12** (see Table 2).

1. 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 with Me_4Si as the internal standard. Mass spectra were obtained with a Kratos MS 30 instrument. Microanalyses were performed at the Faculty of Science, Cairo University, Cairo, Egypt. Solutions were evaporated under diminished pressure unless stated otherwise. TLC was done on silica gel plates using $CHCl_3$–MeOH mixtures.

*5-(*D-arabino*-Tetrahydroxybutyl)-3-(2,3-dihydro-1,3,4-oxadiazole-2-thion-5-yl)-2-methylfuran* (**2**).—To

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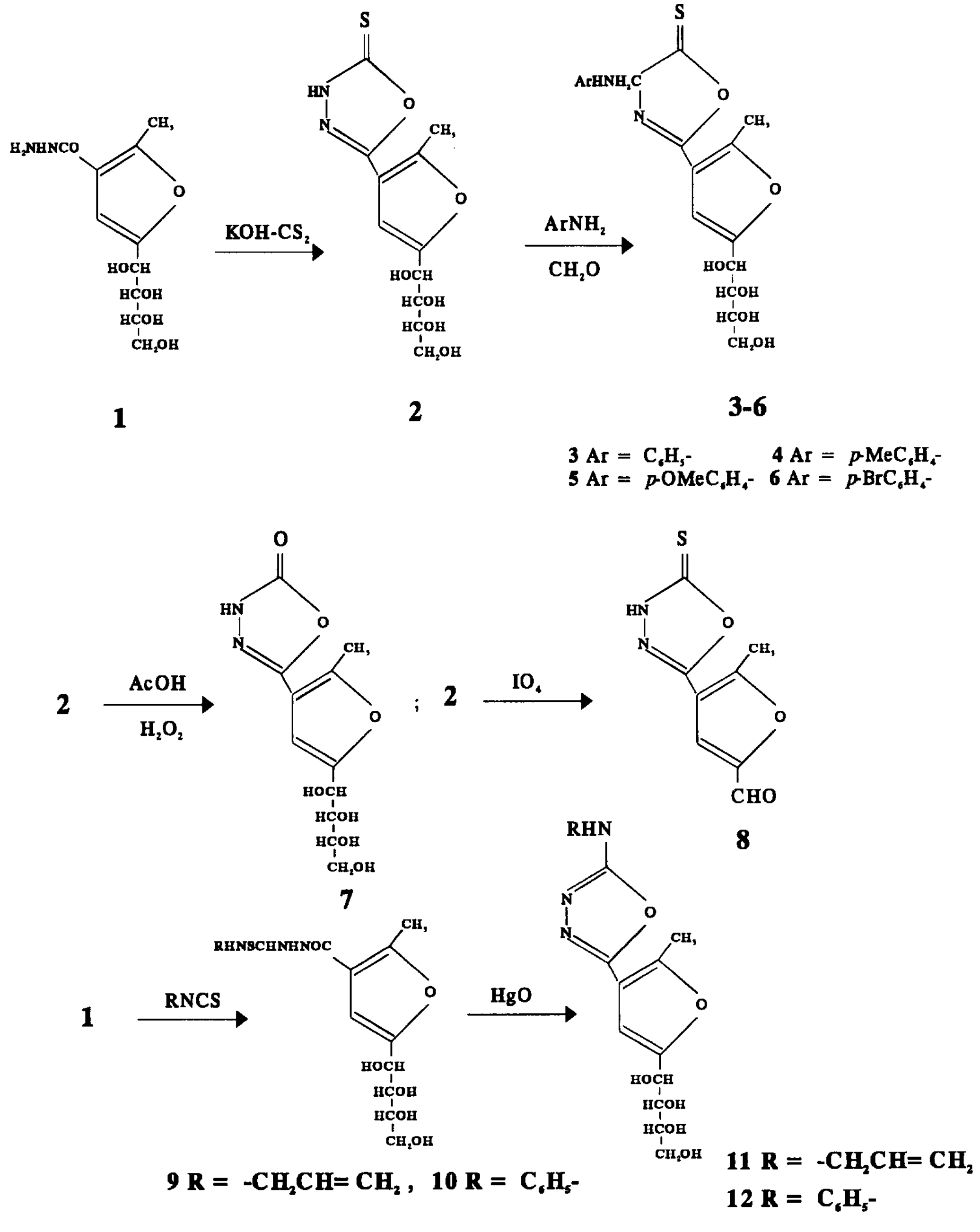
a cold stirred solution of 5-(D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoylhydrazine (5.2 g, 20 mmol) in EtOH (50 mL) containing KOH (1.12 g, 20 mmol), CS_2 (7.6 g, 100 mmol) was added gradually. The mixture was heated under reflux on a steam-bath until H_2S evolution ceased. EtOH was removed by distillation under diminished pressure, the residue was stirred with H_2O, filtered, and the filtrate was neutralized with 10% HCl. The precipitated product was filtered off, washed thoroughly with H_2O, dried, and recrystallized from EtOH (3.5 g, 57.9%), mp 160 °C. γ_{max} (cm^{-1}): 1092 (C=S), 1657 (C=N), 3217 and 3417 (NH, OH). ^1H NMR (Me_2SO-d_6): δ 2.60 (s, 3 H, CH_3), 3.80–4.90 (m, 9 H, carbohydrate residue), 6.65 (s, 1 H, H-4 furan); *m/z* (relative abundance) 50(8.8), 51(12.3), 53(20.9), 55(15.6), 56(19.0), 63(5.3), 64(19.0), 65(7.1), 74(5.3), 76(100.0), 78(10.4), 80(5.9), 121(7.8), 136(14.5), 168(7.8), 194(2.2), 195(25.1), 196(3.7), 210(8.4), 211(93.0), 268(2.9), 284(39.1). Found: C, 43.80; H, 4.67; N, 9.11; $C_{11}H_{14}N_2O_6S$ required: C, 43.70; H, 4.67; N, 9.27.

*5-(*D-arabino*-Tetrahydroxybutyl)-3-(2,3-dihydro-3-(arylaminomethyl)-1,3,4-oxadiazole-2-thion-5-yl)-2-*



Scheme 1.

Table 1
IR Spectral data and analytical data of compounds **3–6**

Compound	Ar.	C=S	C=N	NH, OH	Mp (dec.)	Yield (%)	Molecular formula	Anal. Calcd/Found C	H	N
3	C_6H_5-	1065	1643	3385, 3455	170°	99.0	$C_{18}H_{21}N_3O_6S$	53.06 53.00	5.20 5.30	10.31 10.33
4	*p*-MeC_6H_4-	1086	1643	3347, 3409	103°	83.0	$C_{19}H_{23}N_3O_6S$	54.14 54.20	5.50 5.55	9.97 10.00
5	*p*-$OMeC_6H_4$-	1084	1641	3314, 3435	90°	68.6	$C_{19}H_{23}N_3O_7S$	52.16 52.10	5.30 5.35	9.61 9.65
6	*p*-BrC_6H_4-	1088	1627	3346, 3497	110°	82.2	$C_{18}H_{20}BrN_3O_6S$	44.45 44.45	4.15 4.20	8.64 8.80

methylfuran (**3–6**).—A solution of the required arylamine (0.93 g, 1 mmol) in EtOH (5 mL) was added dropwise to a stirred solution of compound **2** (0.30 g, 1 mmol) in EtOH (10 mL) containing formalin (2 mL, 37%). The mixture was stirred for 3 h at room temperature and then refrigerated overnight. The separated product was filtered off, washed with EtOH, dried, and recrystallized from EtOH as needles. ^1H NMR (Me_2SO-d_6) of compound **4**: δ 2.15 (s, 3 H, CH_3), 4.25–6.05 (m, 11 H, carbohydrate residue and CH_2N), 6.50 (s, 1 H, H-4 furan), 6.55–7.55 (m, 5 H, Ar-H and N-H) (Table 1).

*5-(*D-arabino-*Tetrahydroxybutyl)-3-(2,3,-dihydro-1,3,4-oxadiazole-2-one-5-yl)-2-methylfuran* (**7**).—The title compound was prepared by stirring a solution of compound **2** (1.0 g, 3 mmol) in glacial CH_3COOH (10 mL) with H_2O_2 (5 mL, 30%) for 3 h at room temperature. The mixture was then poured into cold water and the product filtered off, washed with water, and dried. It was recrystallized from EtOH (0.3 g, 30.3%), mp 145 °C (dec). γ_{max} (cm^{-1}): 1642 (C=N), 1690 (C=O), 3369 and 3435 (NH, OH). Found: C, 46.10; H, 4.95; N, 9.80; $C_{11}H_{14}N_2O_7$ required: C, 46.15; H, 4.93; N, 9.79.

3-(2,3-Dihydro-1,3,4-oxadiazole-2-thion-5-yl)-5-formyl-2-methylfuran (**8**).—A solution of **2** (1.5 g, 5 mmol) in distilled water was treated with a slight excess of a saturated solution of $NaIO_4$ (3.5 g, 16 mmol) in distilled H_2O (25 mL) dropwise with stirring for 1 h. The aldehyde derivative that separated out was filtered off, washed with little water, and dried. It was recrystallized from EtOH as needles (0.45 g, 42.8%), mp 109 °C (dec). γ_{max} (cm^{-1}): 1060 (C=S), 1642 (C=N), 1661 (CHO), 3331 (NH). Found: C, 45.70; H, 2.90; N, 13.35; $C_8H_6N_2O_3S$ required: C, 45.71; H, 2.88; N, 13.33.

*1-(5-*D-arabino-*Tetrahydroxybutyl)-2-methylfuro-3-yl)-4-substituted thiosemicarbazide* (**9**, **10**).—A solution of compound **1** (1.3 g, 5 mmol) in EtOH (50 mL) was heated under reflux with substituted isothio-

Table 2
Analytical data of compounds **9–12**

Compound	R	Mp	Yield (%)	Molecular formula	Anal. Calcd/Found C	H	N
9	Allyl	195°	77.9	$C_{14}H_{21}N_3O_6S$	46.78 46.80	5.89 5.90	11.69 11.70
10	Ph	95°	86.0	$C_{17}H_{21}N_3O_6S$	51.63 51.70	5.35 5.20	10.63 10.60
11	Allyl	110°	51.2	$C_{14}H_{19}N_3O_6$	51.69 51.70	5.89 5.98	12.92 13.00
12	Ph	145°	73.8	$C_{17}H_{19}N_3O_6$	56.50 56.60	5.30 5.35	11.63 11.70

cyanate (0.5 g, 5 mmol) for 2 h. After concentration and cooling, the solid deposited was filtered off, washed with a little EtOH, and dried. It was recrystallized from EtOH in needles (Table 2); IR of compound **9**: 1031 (C=S), 1641 (C=N), 1670 (C=O), 3307 and 3451 (NH and OH). IR of compound **10**: 1041 (C=S), 1636 (C=N), 1659 (C=O), 3267 and 3432 (NH and OH). ^{1}H NMR (Me$_2$SO-d_6) of compound **10**: δ 2.49 (s, 3 H, CH$_3$), 4.00–5.20 (m, 9 H, carbohydrate residue), 6.62 (s, 1 H, H-4 furan), 6.80–7.45 (m, 5 H, Ar-H), 9.60 (sh, 1 H, NH), 9.80 (sb, 1 H, NH), 10.90 (sb, 1 H, NHCO).

*5-(*D-arabino*-Tetrahydroxybutyl)-3-(2-substituted amino-1,3,4-oxadiazol-5-yl)-2-methylfuran* (**11** and **12**).—Finely powdered HgO (0.6 g, 32 mmol) was added portionwise over a period of 30 min, to a boiling stirred solution of 1-(5-D-*arabino*-tetrahydroxybutyl)-2-methylfuro-3-yl)-4-substituted thiosemicarbazide (**9** and **10**) (1.1 g, 3 mmol) in EtOH (100 mL). The suspension was stirred and heated under reflux for 3 h. The hot mixture was filtered and the black precipitate was washed with boiling EtOH (10 mL). The combined filtrate and washings were concentrated to small volume, then a few drops of H$_2$O were added and the mixture was left overnight at room temperature to effect complete deposition of the product, which was filtered off, washed, dried, and recrystallized from EtOH (Table 2). IR of compound **11**: 1620 (C=N), 3250–3357 (NH and OH). IR of compound **12**: 1634 (C=N), 3216–3407 (NH and OH); and its ^{1}H NMR (Me$_2$SO-d_6): δ 2.50 (s, 3 H, CH$_3$), 4.15–5.15 (m, 9 H, the sugar part), 6.45 (s, 1 H, H-4 furan), 6.70–7.55 (m, 5 H, Ar-H), 10.40 (sb, 1 H, NH).

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