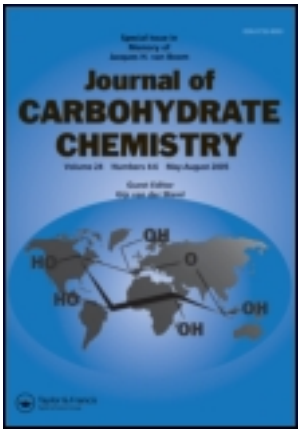

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Synthesis of Novel Galactopyranosyl-Derived Spiro Barbiturates

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Synthesis of Novel Galactopyranosyl-Derived Spiro Barbiturates

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Malonic acid undergoes condensation readily with ureas to yield barbituric acids **2**, which on bromination give 5,5-dibromobarbituric acids **3**. Reaction of α-D-galactose with these 5,5-dibromo barbituric acids afforded 2,3-α-D-galactopyrano-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones **4**. The structures of the products have been assigned on the basis of ^{1}H NMR, ^{13}C NMR, FAB-MS, optical activity, and elemental analysis. The title compounds are found to have antibacterial and antifungal activities.

Keywords Barbituric acid, 5, 5-Dibromo barbituric acid, α-D-Galactose, Dioxolane, Triones

INTRODUCTION

SPIRO systems have been the subject of considerable interest in chemistry because of their unique structural and reactivity pattern. Many spiro compounds possess antiparasitic and analgesic activities.[1] The literature reports revealed the synthesis of spiroheterocycles, which were used as intermediates for aldose reductase inhibitors, and some new spiroheterocycles are also found to have activity as herbicides and pesticides.[2] Spirocarbocyclic systems also enhance the biologic potency of certain compounds.[3] Barbituric acids have been reported to possess a wide spectrum of biologic activities as sedatives and hypnotics, antitumor, antiviral, anti-inflammatory,

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antisclerotics, and bacteriostatics.[4–6] 1,3-Dioxolanes have been used as antispasmodics,[7] sedatives, analgesics, tranquilizers and anesthesis.[8] Drugs modified with carbohydrates exhibit a variety of biologic and therapeutic properties. Certain glycoconjugates are more readily excretable and resistant to significant metabolic transformation.[9–12] In continuation of our work on the synthesis of 2,3-α-D-glucopyrano-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8, 10-triones based on the interaction of α-D-glucopyranose and 5,5-dibromo barbituric acid,[13] herein we report the synthesis and screening results of 2,3-α-D-galactopyrano-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones **4** in antibacterial and antifungal assays.

RESULTS AND DISCUSSION

The barbituric acids **2** were prepared by the Biltz and Wittek method[14] in which ureas **1** are condensed with malonic acid in acetic acid-acetic anhydride. 5,5-Dibromo barbituric acids **3** were prepared by adding bromine to barbituric acids in suitable solvents.[15,16] Glacial acetic acid was found to be the most convenient solvent for bromition of N-substituted barbituric acids. These acids gave a positive test for bromine. The rate of dioxolane formation-etherification depends on the presence of substituents attached to nitrogen atoms in barbituric acids. It is fast in the case of 1-aryl and 1,3-diaryl barbituric acids. The replacement of N-hydrogen by aryl groups increases the solubility of barbituric acids in organic solvents. In the ^{1}H NMR spectrum, **3a** exhibited a singlet for NH at δ 11.68 ppm, while the ^{13}C NMR spectrum showed peaks at 163 (C-6, C-4,), 148 (C-2), and 46 ppm (C-5, C—Br). The IR spectrum showed absorption bands at 3203 (NH), 1714 (C═O), 1183 (C-N-C), and 587 cm^{-1} (C-Br). The reaction of 5,5-dibromo barbituric acid **3a** with α-D-galactose afforded **4a**. The negative test for bromine, the absence of C-Br absorption band in the spectrum, and the presence of strong band at 1263 cm^{-1} for C-O-C is fully consistent with structure of 2,3-α-D-galactopyrano-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones **4a**. The IR spectrum showed characteristic bands at 3131 (OH), 3061 (NH), 2956 (galactosidic CH), 1708 (C═O), 1176 (C-N-C), and 1152 cm^{-1} (C-O) groups. The ^{1}H NMR spectrum of **4a** showed signals at δ 11.72 (s, 1H, N-H), 9.79, (s, 1H, O-H), 5.05–5.12 (m, H-2′, anomeric proton), and 4.68 ppm (d, H-1′, anomeric proton). In the proton-decoupled ^{13}C NMR, the anomeric carbon C-1′ and C-2′ resonated at 102 and 82 ppm, respectively. The FAB-MS spectrum showed a molecular ion peak at 304 (M^+) and was dominated by m/z 126 ($C_4O_3N_2H_2$) with the loss of 178 amu corresponding to the loss of an intact sugar moiety, $C_6H_{10}O_6$. Also, the molecular ion peak at 304 (M^+) confirms the molecular formula $C_{10}O_9N_2H_{12}$. All the compounds gave satisfactory C, H, and N elemental analysis (Table 2).

Table 1: Characterization data of compound 2a–2k.

Product	R	R_1	Mol. Formula	mp (°C)	Yield (%)	%Found (Calcd)		
						C	H	N
2a	H	H	$C_4H_4O_3N_2$	255	50	37.82 (37.50)	3.83 (3.12)	21.98 (21.87)
2b	C_6H_5	H	$C_{10}H_8O_3N_2$	262	48	59.69 (59.40)	3.98 (3.96)	13.93 (13.86)
2c	C_6H_5	C_6H_5	$C_{16}H_{12}O_3N_2$	238	52	69.23 (69.06)	4.54 (4.31)	10.37 (10.07)
2d	*O*-CH_3-C_6H_4	H	$C_{11}H_{10}O_3N_2$	181	44	33.69 (33.41)	2.84 (2.53)	7.39 (7.08)
2e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{18}H_{16}O_3N_2$	210	47	44.91 (44.62)	3.72 (3.30)	5.86 (5.78)
2f	*p*-CH_3-C_6H_4	H	$C_{11}H_{10}O_3N_2$	243	44	33.57 (33.41)	2.91 (2.53)	7.33 (7.08)
2g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{18}H_{16}O_3N_2$	233	49	44.93 (44.62)	3.77 (3.30)	5.85 (5.78)
2h	*O*-OCH_3-C_6H_4	H	$C_{11}H_{10}O_4N_2$	253	41	32.42 (32.11)	2.76 (2.43)	6.97 (6.81)
2i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{18}H_{16}O_5N_2$	186	43	41.96 (41.86)	3.42 (3.10)	5.84 (5.42)
2j	*P*-OCH_3-C_6H_4	H	$C_{11}H_{10}O_4N_2$	190	49	32.47 (32.11)	2.81 (2.43)	6.96 (6.81)
2k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{18}H_{16}O_5N_2$	220	48	41.93 (41.86)	2.81 (3.10)	5.79 (5.42)

Table 2: Characterization data of compounds 4a–4k.

Product	R	R_1	Mol. Formula	mp (°C)	Yield (%)	$(\alpha)_D^{29}$ (°)	% Found (Calcd)		
							C	H	N
4a	H	H	$C_{10}H_{12}O_9N_2$	>285	80	50.72	39.71 (39.47)	3.71 (3.94)	7.44 (7.36)
4b	C_6H_5	H	$C_{10}H_{12}O_9N_2$	164	82	60.71	50.95 (50.52)	4.52 (4.21)	7.48 (7.36)
4c	C_6H_5	C_6H_5	$C_{22}H_{20}O_9N_2$	198	79	67.72	57.94 (57.89)	4.55 (4.38)	6.34 (6.14)
4d	*O*-CH_3-C_6H_4	H	$C_{17}H_{17}O_9N_2$	228	82	100.67	51.95 (51.64)	4.66 (4.56)	7.12 (7.08)
4e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{24}H_{24}O_9N_2$	252	78	113.38	59.18 (59.50)	4.72 (4.95)	5.91 (5.78)
4f	*p*-CH_3-C_6H_4	H	$C_{17}H_{17}O_9N_2$	105	81	−91.72	51.76 (51.64)	4.77 (4.56)	7.18 (7.08)
4g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{24}H_{24}O_9N_2$	265	79	72.47	59.22 (59.50)	4.77 (4.95)	5.90 (5.78)
4h	*O*-OCH_3-C_6H_4	H	$C_{17}H_{18}O_{10}N_2$	137	80	46.29	49.51 (49.75)	4.33 (4.14)	6.98 (6.82)
4i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{24}H_{24}O_{11}N_2$	118	81	35.85	55.62 (55.81)	4.90 (4.65)	5.77 (5.42)
4j	*P*-OCH_3-C_6H_4	H	$C_{17}H_{18}O_{10}N_2$	166	76	129.68	49.53 (49.75)	4.31 (4.14)	6.96 (6.82)
4k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{24}H_{24}O_{11}N_2$	270	82	−54.34	55.64 (55.81)	4.87 (4.65)	5.76 (5.42)

MICROBIAL ACTIVITY

Antimicrobial Activity

The synthesized compounds were screened for their antibacterial activities by the using the cup-plate method against *Bacillus subtilis* (gram-positive) and *Escherichia coli* (gram-negative) at concentrations of 100 μg/mL in DMF. Pure norfloxacin was taken as standard antibiotic for the comparison of the results. The sterilized nutrient agar media (30 mL) was inoculated with the test organism and poured optically into the Petridishes. Then four holes of 6-mm diameter were punched carefully by the using sterile cork-border and these were completely filled with different test solution. The plates were then incubated for 24 h at 37°C and zones of inhibitions were measured. Similar procedure was adopted for pure norfloxacin and the corresponding zone diameters were compared. The screening results indicate that compounds **4a–k** showed moderate to excellent bactericidal activities against both organisms (Table 3).

Table 3: Data for in vitro antibacterial and antifungal activities of compounds 4a–k.

	Diameter of Inhibition Zone (in mm) Against			
	Bacterial Strains		Fungal Strains	
Products	***E. coli***	***B. subtilis***	***A. niger***	***C. albicans***
4a	15	17	21	23
4b	14	16	17	15
4c	10	09	11	—
4d	12	10	15	13
4e	16	14	24	28
4f	13	13	17	—
4g	14	16	22	18
4h	11	14	16	16
4i	15	13	23	21
4j	13	11	—	17
4k	14	16	22	22

— = no inhibition of growth.
Diameter of zone of inhibition from 13–16 (in mm) shows excellent activity and that of 9–12 (in mm) exhibits moderate activity for bacterial strains.
Diameter of zone of inhibition from 22–28 (in mm) shows excellent activity, that of 15–21 (in mm) exhibits moderate activity, and that of 11–14 (in mm) shows poor activity for fungal strains.
Norfloxacin 100 μg/mL used as standard against *E. coli* and *B. subtilis*; diameter of zone of inhibition is 20.
Griseofulvin 100 μg/mL used as standard against *A. niger* and *C. albicans*; diameter of zone of inhibition is 32.

Antifungal Activity

The antifungal activity of synthesized compounds was evaluated by the using above same method (cup-plate technique) against *Aspergillus niger* and *Candida albicans* at a concentration 100 μg/mL in DMF. The plates were incubated for 8 days at 37°C. The zones of inhibitions were measured. Similarly, a commercial fungicide griseofulvin was also tested under similar condition with a view of comparing the results. The compounds showed significant fungitoxicity against both the test fungi (Table 3).

EXPERIMENTAL

General Methods

Substituted ureas **1** were prepared as described in the literature.[17] Melting points were determined in open glass capillaries and are uncorrected. Optical rotations were measured at 29°C. Elemental analysis ware determined using the Perkin Elmer 2400 CHN analyzer. FT-IR spectra were recorded using (KBr) disc on Perkin-Elmer spectrum Rx-I spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on Brucker AC-300 F (300 MHz) NMR spectrometer by using DMSO and $CDCl_3$ as solvent and tetramethylsilane as an internal standard. Mass spectra were recorded on 70-S Mass spectrometer using *m*-nitro benzyl alcohol (NBA) matrix.

Barbituric acid 2a. Urea **1a** (0.9 g, 0.015 mol) and malonic acid (2.08 g, 0.02 mol) are dissolved in 5 mL of glacial acetic acid in a flask fitted with dropping funnel, reflux condenser, and stirrer. The mixture was heated to 65°C and 4 mL of acetic anhydride was added during 30 min. The reaction mixture was heated with stirring at 90°C for 3 h. The solvent was removed by distillation under vacuum at 60°C and the residue was treated with 0.2 N NaOH. The clear solution was acidified with 0.2 N HCl to obtain barbituric acid **2a**. mp 255°C (water) (yield 50%).

Similarly, 1-aryl and 1,3-diaryl barbituric acids **(2b–k)** were prepared by the reaction of substituted ureas **(1b–k)** with malonic acid. Compounds gave satisfactory C, H, and N analysis (Table 1).

5,5-Dibromobarbituric acid 3a. This was prepared by adding molecular bromine (2.55 g, 0.016 mol) to barbituric acids **2a** (1.28 g, 0.01 mol) in H_2O (60 mL) at 50°C. mp 235°C (aq MeOH) (yield 70%); IR (KBr): 3203 (-NH), 1714 (C═O), 1183 (C-N-C), 587 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.68 (s, N-H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 163 (C-4, C-6), (s, C═O), 148 (C-2) (s, C═O), 46 (C-5) (C-Br). Anal. Calcd. for C, 16.78; H, 0.69; N, 9.79. Found: C, 16.93; H, 1.03; N, 9.97%.

Similarly, 5,5-dibromo-1-aryl-and 1,3-diaryl barbituric acids **(3b–k)** were prepared by adding bromine to 1-aryl and 1,3-diaryl barbituric acids **(2b–k)** in suitable solvents.

5,5-Dibromo-1-phenyl barbituric acid 3b. mp 184°C (AcOH) (yield 68%); IR (KBr): 3181 (-NH), 3056 (Ar-CH), 1731 (C=O), 1179 (C-N-C), 710 (Ar-H), 574 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.53 (s, 1H, N-H); 6.5–9.1 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 161 (C-4) (s, C=O), 158 (C-6) (s, C=O), 150 (C-2) (s, C=O), 47 (C-5) (C-Br). Anal. Calcd. for C, 33.14; H, 1.65; N, 7.73. Found: C, 33.54; H, 1.89; N, 7.93%.

5,5-Dibromo-1,3-diphenyl barbituric acid 3c. mp 152°C (benzene) (yield 71%); IR (KBr): 3071 (Ar-CH), 1720 (C=O), 1181 (C-N-C), 714 (Ar-H), 579 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 6.5–9.0 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 159 (C-4) (s, C=O), 157 (C-6) (s, C=O), 151 (C-2) (s, C=O), 46 (C-5) (C-Br). Anal. Calcd. for C, 43.83; H, 2.28; N, 6.69. Found: C, 43.97; H, 2.59; N, 6.74%.

5,5-Dibromo-1-*o*-tolyl barbituric acid 3d. mp 174°C (AcOH) (yield 69%); IR (KBr): 3184 (-NH), 3049 (Ar-CH), 1733 (C=O), 1178 (C-N-C), 710 (Ar-H), 576 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.23 (s, 1H, N-H), 6.5–9.1 (m, 5H, Ar-H), 2.32 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 163 (C-4) (s, C=O), 156 (C-6) (s, C=O), 149 (C-2) (s, C=O), 49 (C-5) (C-Br), 21 (Ar-CH_3). Anal. Calcd. for C, 23.78; H, 1.44; N, 5.04. Found: C, 23.89; H, 1.79; N, 5.39%.

5,5-Dibromo-1,3-di-*o*-tolyl barbituric acid 3e. mp 190°C (ethanol) (yield 71%); IR (KBr): 3023 (Ar-CH), 1730 (C=O), 1175 (C-N-C), 715 (Ar-H), 580 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 6.5–9.0 (m, 10H, Ar-H), 2.29 (s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 160 (C-4) (s, C=O), 159 (C-6) (s, C=O), 154 (C-2) (s, C=O), 46 (C-5) (C-Br), 19 (Ar-CH_3). Anal. Calcd. for C, 32.54; H, 2.17; N, 4.34. Found: C, 32.82; H, 2.41; N, 4.67%.

5,5-Dibromo-1-*o*-anisyl barbituric acid 3 h. mp 181°C (AcOH) (yield 74%); IR (KBr): 3186 (-NH), 3059 (Ar-CH), 1747 (C=O), 1175 (C-N-C), 710 (Ar-H), 575 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.33 (s, 1H, N-H), 6.5–9.0 (m, 5H, Ar-H), 3.79 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 164 (C-4) (s, C=O), 157 (C-6) (s, C=O), 152 (C-2) (s, C=O), 59 (Ar-OCH_3), 48 (C-5) (C-Br). Anal. Calcd. for C, 23.11; H, 1.40; N, 4.90. Found: C, 23.37; H, 1.73; N, 4.98%.

5,5-Dibromo-1,3-di-*o*-anisyl barbituric acid 3i. mp 164°C (AcOH) (yield 72%); IR (KBr): 3063 (Ar-CH), 1734 (C=O), 1175 (C-N-C), 715 (Ar-H), 571 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 6.5–9.0 (m, 10H, Ar-H), 3.82 (s, 6H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 162 (C-4) (s, C=O), 154 (C-6) (s, C=O), 150 (C-2) (s, C=O), 57 (Ar-OCH_3), 49 (C-5) (C-Br). Anal. Calcd. for C, 31.95; H, 2.07; N, 4.14. Found: C, 31.99; H, 2.37; N, 4.34%.

2,3-α-D-Galactopyrano-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones 4a. A mixture of 5,5-dibromo barbituric acid **3a** (2.85 g, 0.01 mol), α-D-galactose (1.80 g, 0.01 mol), pyridine (0.79 g, 0.01 mol), and alcohol (25 mL) was

refluxed for 3 h. The excess of solvent was distilled off and the syrup poured onto crushed ice to obtain **4a**. mp >285°C (AcOH) (yield 80%); IR (KBr): 3131 (-OH), 3061 (-NH), 2956 (galactosidic-CH), 1708 (C=O), 1263 (C-O-C), 1176 (C-N-C), 1152 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.72 (s, 1H, N-H); 9.79 (s, 1H, O-H), 5.5–5.3 (m, 2H, 3′and 4′-H); 5.05–5.12 (m,1H, 2′-H, anomeric proton), 4.68 (d, 1H, 1′-H, anomeric proton), 4.11 (dd, 2H, 6′-H_2), 3.77–3.82 (m, 1H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 165 (C-6) (s, C=O), 163 (C-4) (s, C=O), 148 (C-2) (s, C=O), 119 (C-5, spiro C-atom), 102 (C-1′, anomeric C-atom), 82 (C-2′, anomeric C-atom), 78 (C-5′), 75 (C-3′), 62 (C-4′), 55 (C-6′); FAB-MS: m/z 304 (M^+, $C_{10}O_9N_2H_{12}$), 126 ($C_4O_3N_2H_2$). Anal. Calcd. for C, 39.47; H, 3.94; N, 7.44. Found: C, 39.71; H, 3.72; N, 7.44%.

When the reaction of α-D-galactopyranose was extended with several other 5,5-dibromo- 1-aryl-and 1,3-diaryl barbituric acids **(3b–k),** then corresponding 2,3-α-D-galactopyrano-1,4-dioxo-7-aryl-7,9-diaza and 7,9-diaryl-7,9-diaza-spiro[4,5]deca-6,8,10-triones **(4b–k)** have been synthesized.

2,3-α-D-Galactopyrano-7-phenyl-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8, 10-triones 4b. IR (KBr): 3178 (-NH), 3201 (-OH), 3052 (Ar-CH), 2861 (galactosidic-CH), 1728 (C=O), 1268 (C-O-C), 1172 (C-N-C), 1158 (C-O), 710 (Ar-H); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.31 (s, N-H), 9.81 (s, O-H), 6.5–8.5 (m, 5H, Ar-H), 5.5–5.2 (m, 2H, 3′and 4′-H), 5.03–5.11 (m,1H, 2′-H, anomeric proton), 4.62 (d, 1H, 1′-H, anomeric proton), 4.09 (dd, 2H, 6′-H_2), 3.76–3.84 (m, 1H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 162 (C-4) (s, C=O), 160 (C-6) (s, C=O), 154 (C-2) (s, C=O), 120–160 (aromatic C-atom), 118 (C-5, spiro C-atom), 103 (C-1′, anomeric C-atom), 85 (C-2′, anomeric C-atom), 77 (C-5′), 75 (C-3′), 64 (C-4′), 57 (C-6′); FAB-MS: m/z 380 (M^+, $C_{16}O_9N_2H_{16}$), 202 ($C_{10}O_3N_2H_6$), 125 ($C_4O_3N_2H$).

2,3-α-D-Galactopyrano-7,9-diphenyl-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones 4c. IR (KBr): 3244 (-OH), 3048 (Ar-CH), 2912 (galactosidic-CH), 1730 (C=O), 1270 (C-O-C), 1169 (C-N-C), 1151 (C-O), 719 (Ar-H); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 9.66 (s, 1H, O-H), 6.5–8.5 (m, 5H, Ar-H), 5.5–5.3 (m, 2H, 3′and 4′-H); 5.02–5.09 (m, 1H, 2′-H, anomeric proton), 4.66 (d, 1H, 1′-H, anomeric proton), 4.10 (dd, 2H, 6′-H_2), 3.79–3.84 (m, 1H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 164 (C-4) (s, C=O) 162 (C-6) (s, C=O), 149 (C-2) (s, C=O), 120–160 (aromatic C-atom), 118 (C-5, spiro C-atom), 103 (C-1′, anomeric C-atom), 83 (C-2′, anomeric C-atom), 76 (C-5′), 74 (C-3′), 62 (C-4′), 54 (C-6′); FAB-MS: m/z 456 (M^+, $C_{22}O_9N_2H_{20}$), 278 ($C_{16}O_3N_2H_{10}$), 201 ($C_{11}O_3N_2H_5$), 124 ($C_2O_3N_2$).

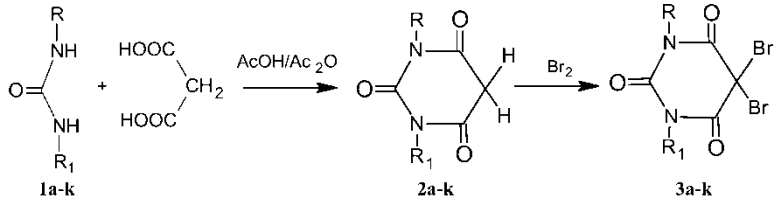
2,3-α-D-Galactopyrano-7-*o*-tolyl-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8, 10-triones 4d. IR (KBr): 3211 (-OH), 3180 (-NH), 3052 (Ar-CH), 2864 (galactosidic-CH), 1731 (C=O), 1265 (C-O-C), 1175 (C-N-C), 1159 (C-O), 710 (Ar-H); ^{1}H

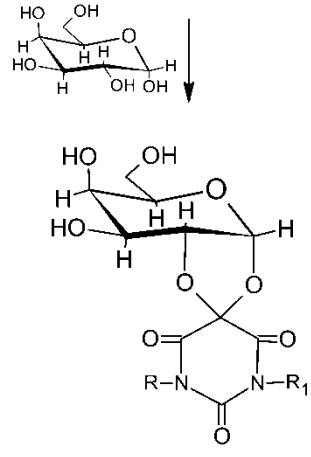
NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.27 (s, N-H), 9.79 (s, O-H), 6.5–8.5 (m, 4H, Ar-H), 5.6–5.2 (m, 2H, 3′and 4′-H), 5.03–5.13 (m, 1H, 2′-H, anomeric proton), 4.62 (d, 1H, 1′-H, anomeric proton), 4.09 (dd, 2H, 6′-H_2), 3.75–3.80 (m, 1H, 5′-H), 2.23 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 162 (C-4) (s, C═O), 160 (C-6) (s, C═O), 154 (C-2) (s, C═O), 120–160 (aromatic C-atom), 119 (C-5, spiro C-atom), 103 (C-1′, anomeric C-atom), 87 (C-2′, anomeric C-atom), 79 (C-5′), 72 (C-3′), 65 (C-4′), 58 (C-6′), 20 (Ar-CH_3); FAB-MS: m/z 394 (M^+, $C_{17}O_9N_2H_{18}$), 216 ($C_{11}O_3N_2H_8$), 201 ($C_{10}O_3N_2H_5$), 125 ($C_4O_3N_2H$).

2,3-α-D-Galactopyrano-7,9-di-*o*-tolyl-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones 4e. IR (KBr): 3214 (-OH), 3061 (Ar-CH), 2890 (galactosidic-CH), 1729 (C═O), 1269 (C-O-C), 1173 (C-N-C), 1148 (C-O), 710 (Ar-H); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.23 (s, N-H), 9.79 (s, O-H), 6.5–8.5 (m, 8H, Ar-H), 5.5–5.1 (m, 2H, 3′and 4′-H); 5.03–5.11 (m,1H, 2′-H, anomeric proton), 4.69 (d,1H,1′-H, anomeric proton), 4.11 (dd, 2H, 6′-H_2), 3.73–3.79 (m, 1H, 5′-H), 2.30 (s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 164 (C-4) (s, C═O), 161 (C-6) (s, C═O), 157 (C-2) (s, C═O), 120–160 (aromatic C-atom), 119 (C-5, spiro C-atom), 103 (C-1′, anomeric C-atom), 89 (C-2′, anomeric C-atom), 78 (C-5′), 73 (C-3′), 64 (C-4′), 55 (C-6′), 20 (Ar-CH_3); FAB-MS: m/z 484 (M^+, $C_{24}O_9N_2H_{24}$), 306 ($C_{18}O_3N_2H_{14}$), 291 ($C_{17}O_3N_2H_{11}$), 215 ($C_{11}O_3N_2H_7$), 200 ($C_{10}O_3N_2H_4$), 124 ($C_4O_3N_2$).

2,3-α-D-Galactopyrano-7-*o*-anisyl-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8, 10-triones 4 h. IR (KBr): 3219 (-OH), 3184 (-NH), 3054 (Ar-CH), 2871 (galactosidic-CH), 1744 (C═O), 1269 (C-O-C), 1174 (C-N-C), 1146 (C-O), 710 (Ar-H); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.31 (s, N-H), 9.81 (s, O-H), 6.5–8.5 (m, 5H, Ar-H), 5.6–5.2 (m, 2H, 3′and 4′-H), 5.03–5.16 (m, 1H, 2′-H, anomeric proton), 4.67 (d, 1H, 1′-H, anomeric proton), 4.12 (dd, 2H, 6′-H_2), 3.78–3.83 (m, 1H, 5′-H), 3.92 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 166 (C-4) (s, C═O), 163 (C-6) (s, C═O), 158 (C-2) (s, C═O), 120–160 (aromatic C-atom), 119 (C-5, spiro C-atom), 102 (C-1′, anomeric C atom), 87 (C-2′, anomeric C-atom), 78 (C-5′), 73 (C-3′), 66 (C-4′), 59 (C-6′), 57 (CH_3, Ar-OCH_3); FAB-MS: m/z 410 (M^+, $C_{17}O_{10}N_2H_{18}$), 232 ($C_{11}O_4N_2H_8$), 201 ($C_{10}O_3N_2H_5$), 125 ($C_4O_3N_2H$).

3-α-D-Galactopyrano-7,9-di-*o*-anisyl-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones 4i. IR (KBr): 3212 (-OH), 3059 (Ar-CH), 2868 (galactosidic-CH), 1737 (C═O), 1271 (C-O-C), 1172 (C-N-C), 1153 (C-O), 710 (Ar-H); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): 11.39 (s, N-H), 9.87 (s, O-H), 6.5-8.5 (m, 8H, Ar-H), 5.6–5.2 (m, 2H, 3′and 4′-H), 5.03–5.13 (m, 1H, 2′-H, anomeric proton), 4.65 (d, 1H, 1′-H, anomeric proton), 4.12 (dd, 2H, 6′-H_2), 4.03 (s, 6H, OCH_3), 3.78 (m, 1H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): 166 (C-4) (s, C═O), 163 (C-6) (s, C═O), 158 (C-2) (s, C═O), 120–160 (aromatic





4a-k

	R	R_1
a)	H	H
b)	Phenyl	H
c)	Phenyl	Phenyl
d)	*o*-tolyl	H
e)	*o*-tolyl	*o*-tolyl
f)	*p*-tolyl	H
g)	*p*-tolyl	*p*-tolyl
h)	*p*-anisyl	H
i)	*o*-anisyl	*o*-anisyl
j)	*p*-anisyl	H
k)	*p*-anisyl	*p*-anisyl

Scheme 1

C-atom), 119 (C-5, spiro C-atom), 102 (C-1′, anomeric C-atom), 87 (C-2′, anomeric C-atom), 78 (C-5′), 73 (C-3′), 66 (C-4′), 59 (C-6′), 56 (CH_3, Ar-OCH_3); FAB-MS: m/z 516 (M^+, $C_{24}O_{11}N_2H_{24}$), 338 ($C_{18}O_5N_2H_{14}$), 307 ($C_{17}O_4N_2H_{11}$), 231 ($C_{11}O_4N_2H_7$), 200 ($C_{10}O_3N_2H_4$), 124 ($C_4O_3N_2$) (Scheme 1).

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