Synthesis of Novel Spiro Barbiturates and Their Glycosides

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Abstract:

Malonic acid undergoes condensation readily with ureas**1** to yield barbituric acids **2** which on bromination give5,5-dibromobarbituric acids **3**. Reaction of Pyrogallol with these 5,5-dibromo barbituric acids afforded 2, 3-(4/- Hydroxyl benz)-1, 4-dioxo-7, 9-diaza [4, 5] deca-6, 8, 10-triones. **4**. The compound **4** were glucosylated using acetobromoglucose (ACBG) as a glucosylating agent. to get 2, 3-(3/-*O*-β-D-Glucopyranosyloxybenz)-1,4-dioxo-7,9-diaza-spiro[4,5] deca-6, 8, 10-triones **6.** 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.

Key words: Barbituric acid, 5, 5-dibromo barbituric acid, pyrogallol, 1,3, benzodioxole, glucopyranosyl, triones.

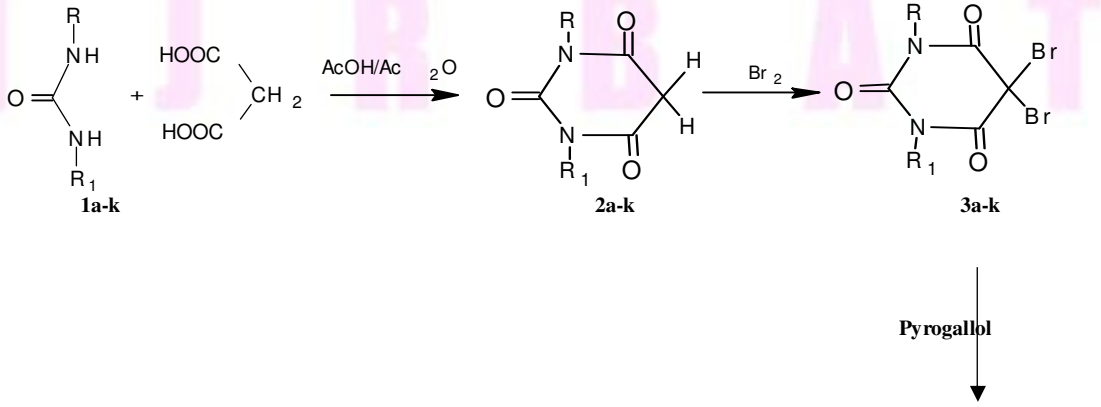
Introduction:

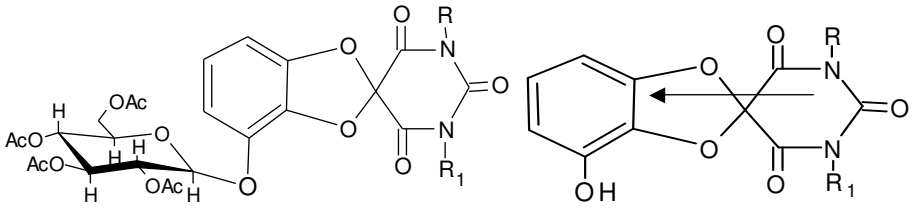
SPIRO systems have been the subject of considerable interest in chemistry because of their unique structural and reactivity pattern. Many spiro compounds possess antiparasitic and analgesic activities.[1] The literature reports revealed the synthesis of spiroheterocycles which were used as intermediates for aldose reductase inhibitors, and some new spiroheterocycles are also found to have activity as herbicides and pesticides.[2]Spirocarbocyclic systems also enhance the biological potency of certain compounds.[3]Barbituric acids have been reported to possess a wide spectrum of biological activities as sedatives and hypnotics, antitumor, antiviral, anti-inflammatory, antisclerotics, and bacteriostatics.[4-6] 1,3, benzodioxole have been used as antispasmodics, sedatives, analgesic, tranquilizer and anesthesia.[7,8] Drugs modified with carbohydrates exhibit a variety of biological 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- (4/- Hydroxyl benz)-1, 4-dioxo-7, 9-diaza [4, 5] deca-6, 8, 10-triones **4** based on the interaction of Pyrogallol and 5,5-dibromo barbituric acid,[13] . The interaction of potassium salt of **4 a** and acetobromoglucose (ACBG) afforded 2, 3-(3/-(2, 3, 4, 6-Tetra-*O*-acetyl-*O*-β-D-glucopyranosyloxybenz))-1, 4-dioxo-7, 9-diaza-spiro[4,5] deca-6, 8, 10-triones **5** which was finally deacetylated using sodium methoxide in methanol to gives 2, 3-(3/-*O*-β-D-Glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5] deca-6, 8, 10-triones **6.** and herein we report the synthesis screening results of 2, 3-(3/-*O*-β-D-Glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5] deca-6, 8, 10-triones **6** inantibacterial and antifungal assays.

Results and Discussion:

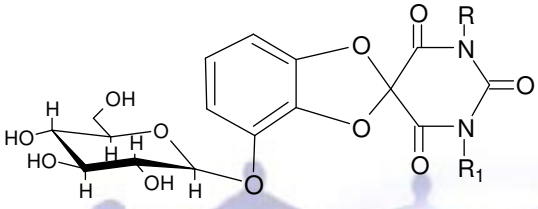
In Biltz and Wittekmethod[14], ureas**1** are condensed with malonic acid in acetic acid-acetic anhydride.to get barbituric acids **2.** The 5,5-Dibromo barbituric acids **3** were prepared by adding bromine to barbituric acids in suitable solvents.[15,16] Glacial acetic acid was found to be the most 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 pyragallol 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 **4a.** The infrared spectrum of **4a** exhibited characteristic bands at 3414 (OH), 3128 (NH), 2931 (Ar-CH), 1645 (C=O), 1218 (C-O-C), 1169 cm^{-1} (C-N-C) groups ^{1}H NMR[156-161]: ^{1}H NMR spectrum of **4a** showed signals at δ 10 (H, NH), 6.18-6.22 (H, Ar-H) and 5.0 (H, OH) groups. The IR of **6a** exhibited characteristics bands at 3549 (glucosidic OH), 3297 (NH), 2913 (Ar-CH), 1706 (C=O), 1282 (C-O-C), 1193 cm^{-1}(C-N-C) ^{1}H NMR: ^{1}H NMR spectrum of **6a** showed signals at δ 10 (H, NH), 6.2-6.66 (H, Ar-H) 3.7 (H, CH_2), 3.4-5.8 (H, glucosidic CH)and 2 ppm (H, glucosidic CH). EI-Mass spectrum showed a molecular ion peak at 412 (M^+) and was dominated by m/z 250 ($C_{13}O_{11}N_2H_{18}$) with the loss of $C_6H_{10}O_6$. (fig 1.22). It showed molecular ion peaks at m/z 233, 120, 108, 92 and 78. In view of above the facts, the compound **6a** was assigned the structure 2,3-(3/-*O*-β-D-Glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones. All the compounds gave satisfactory C, H, and N elemental analysis (Table V).





5a-k 4a-k

CH_3ONa/CH_3OH



6a-k

Scheme- I

	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

MICROBIAL ACTIVITY

2.1.1. Antimicrobial activity

The synthesized compounds were screened for their antibacterial activities by the using the cup-plate method against B. *subtilis* (gram-positive) and E. *coli* (gram-negative) at concentrations of 100 µg/mL in DMF. Pure Norfloxacine 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 in to 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^{0}C and zones of inhibitions were measured. Similar procedure was adopted for pure Norfloxacine and the corresponding zone diameters were compared. The screening results

indicate that compounds **6a-k** showed moderate to excellent bactericidal activities against both organisms (Table VI).

Antifungal activity

The antifungal activity of synthesized compounds was evaluated by the using above same method (cup-plate technique) against A. *niger* and C. *albicans* at concentration 100 µg/mL in DMF. The plates were incubated for 8 days at 37^{0}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 VI).

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^{0}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 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^{0}C and 4 mL of acetic anhydride was added during 30 min. The reaction mixture was heated with stirring at 90^{0}C for 3 h. The solvent was removed by distillation under vacuum at 60^{0}C and the residue was treated with 0.2 N NaOH. The clear solution was acidified with 0.2 N HCl to obtained barbituric acid **2a**. mp 255^{0}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 I).

5,5-Dibromobarbituric acid 3a. Thiswas prepared by adding molecular bromine (2.55 g, 0.016 mol) to barbituric acids **2a** (1.28 g, 0.01mol) in H_2O (60 mL) at 50^{0}C. mp 235^{0}C (aqMeOH) (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. (Table II)

2, 3- (4/- Hydroxyl benz)-1, 4-dioxo-7, 9-diaza [4, 5] deca-6, 8, 10-triones 4a. A mixture of 5,5-dibromo barbituric acid **3a** (2.85 g, 0.01mol), Pyrogallol (0.01mol), 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 on to crushed ice to obtain **4a.**mp>285 ^{0}C (AcOH) (Yield 80 %); IR (KBr): FT-IR[156-161]: The infrared spectrum of **1a** exhibited characteristic bands at 3414 (OH), 3128 (NH), 2931 (Ar-CH), 1645 (C=O), 1218 (C-O-C), 1169 cm^{-1} (C-N-C) groups H NMR[156-161]: ^{1}H NMR spectrum: δ 10 (H, NH), 6.18-6.22 (H, Ar-H) and 5.0 (H, OH) groups

when the reaction of pyrogallol was extended with several other 5,5-dibromo- 1-aryl-and 1,3-diaryl barbituric acids **(3b-k),** thencorresponding 2, 3- (4/- Hydroxyl benz)-1, 4-dioxo-7, 9-diaza [4, 5] deca-6, 8, 10-triones **(4b-k)** have been synthesized. (Table III)

3-(2, 3, 4, 6-Tetra-O-acetyl-O-β-D-glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-trione 5a: A solution of potassium salt of 3-Hydroxymethyl-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones **4a** (1.3 g) in 5% methanolic KOH (10 mL) was added dropwise to a solution of α-acetobromoglucose (5 g) in dry acetone (20mL). The resulting mixture was stirred at 0^0 C for 8 h, and the reaction was allowed to proceed for an additional

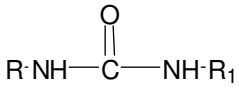
24 h at room temperature, and the solvent was removed under reduced pressure. The resulting brown syrup was dissolved in CH_2OH-CH_2Cl_2 (8:2) and chromatographed on 60-120 mesh silica gels. The reaction was monitored by TLC (R*f* =0.18). The solvent was evaporated. A brown syrupy 3-(2, 3, 4, 6-tetra-*O*-acetyl-*O*-β-D-glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones **5a** was obtained , yield (64%). The compound was found to be optically active and its specific rotation $[\alpha]_D^{29}$ in methanol was found to be 52.72^0.

Likewise, various substituted 3-(2, 3, 4, 6-tetra-O-acetyl-O-β-D-glucopyranosyloxybenz)-1, 4-dioxo-7-aryl-7, 9-diaza-/ 7, 9-diaryl-7, 9-diaza-spiro [4, 5] deca-6, 8, 10-triones **5b-k** were prepared (Table-IV).

2, 3-(*O*-β-D-Glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-trione 6a: A mixture of 3-(2, 3, 4, 6-tetra-*O*-acetyl-*O*-β-D-glucopyranosyloxymethyl)-1, 4-dioxo-7, 9-diaza-spiro[4,5]deca-6, 8, 10-triones **5a** (4.2 g), 5% sodium methoxide (20 mL) and methanol (30 mL) was stirred at room temperature for 2 h, and mixture was allowed to stand at room temperature for 24 hours.. After completion of reaction, which was monitored by TLC (Rf = 0.15), it was neutralized with ion-exchange resin (AmberliteIR 120, sd fine, H^+ form). The reaction mixture was filtered and concentrated in vacuo, to afford a viscous, highly hygroscopic brown syrupy **6a** in moderate yield (80%). The compound was found to be optically active and its specific rotation $[\alpha]_D^{29}$ in methanol was found to be 41.33^0. FT-IR[156-161]: The IR exhibited characteristics bands at 3549 (glucosidicOH), 3297 (NH), 2913 (Ar-CH), 1706 (C=O), 1282 (C-O-C), 1193 cm^{-1}(C-N-C). ^{1}H NMR: ^{1}H NMR spectrum showed signals at δ 10 (H, NH), 6.2-6.66 (H, Ar-H) 3.7 (H, CH_2), 3.4-5.8 (H, glucosidic CH)and 2 ppm (H, glucosidic CH) EI MS[156-161]:EI-Mass spectrum showed a molecular ion peak at 412 (M^+) and was dominated by m/z 250 ($C_{13}O_{11}N_2H_{18}$) with the loss of $C_6H_{10}O_6$. It showed molecular ion peaks at m/z 233, 120, 108, 92 and 78.

In the same manner, various substituted 3-(O-β-D-glucopyranosyloxymethyl)-1, 4-dioxo-7-aryl-7, 9-diaza-/ 7, 9-diaryl-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones **6b-k** were prepared (Table-V).

Table 1 Characterization data of urea and 1-aryl-/ 1,3-diaryl ureas 1a-k

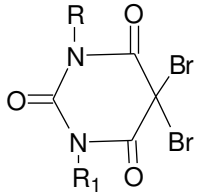


Product	R	R_1	Formula	Mol.M.P. (^{0}C)
1a	H	H	CH_4ON_2	132
1b	C_6H_5	H	$C_7H_6ON_2$	147[a]
1c	C_6H_5	C_6H_5	$C_{13}H_{10}ON_2$	242[b]
1d	*O*-CH_3-C_6H_4	H	$C_8H_8ON_2$	198[a]
1e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{15}H_{14}ON_2$	253[b]
1f	*p*-CH_3-C_6H_4	H	$C_8H_8ON_2$	180[a]
1g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{15}H_{14}ON_2$	254[b]
1h	*O*-OCH_3-C_6H_4	H	$C_8H_8O_2N_2$	168[a]
1i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{15}H_{14}O_3N_2$	184[b]
1j	*P*-OCH_3-C_6H_4	H	$C_8H_8O_2N_2$	168[a]
1k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{15}H_{14}O_3N_2$	234[b]

a = Compounds crystallized from water.

b = Compounds crystallized from glacial acetic acid.

Table II Characterization data 5,5-dibromobarbituric acid and 1-aryl-/ 1,3-diaryl-5,5-dibromo barbituric acids 3a-k



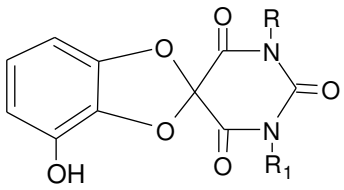
Product	R	R_1	Mol. Formula	M.P. (^{0}C)	Yield (%)	% found(Calcd) C	H	N
3a	H	H	$C_4H_2O_3N_2Br_2$	235 [a]	70	16.91 (16.78)	1.03 (0.69)	9.97 (9.79)
3b	C_6H_5	H	$C_{10}H_6O_3N_2Br_2$	184[b]	68	33.54 (33.14)	1.89 (1.65)	7.93 (7.73)
3c	C_6H_5	C_6H_5	$C_{16}H_{10}O_3N_2Br_2$	152 [c]	71	43.97 (43.83)	2.59 (2.28)	6.74 (6.39)
3d	*O*-CH_3-C_6H_4	H	$C_{11}H_8O_3N_2Br_2$	174 [b]	69	23.89 (23.78)	1.79 (1.44)	5.39 (5.04)
3e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{18}H_{14}O_3N_2Br_2$	190 [a]	71	33.82 (32.54)	2.41 (2.17)	4.67 (4.34)
3f	*p*-CH_3-C_6H_4	H	$C_{11}H_8O_3N_2Br_2$	105 [b]	69	23.87 (23.78)	1.81 (1.44)	5.42 (5.04)
3g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{18}H_{14}O_3N_2Br_2$	265 [b]	75	33.83 (32.54)	2.43 (2.17)	4.66 (4.34)
3h	*O*-OCH_3-C_6H_4	H	$C_{11}H_8O_4N_2Br_2$	181[c]	74	23.37 (23.11)	1.73 (1.40)	4.98 (4.90)
3i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{18}H_{14}O_4N_2Br_2$	164 [b]	72	31.99 (31.95)	2.37 (2.07)	4.34 (4.14)
3j	*P*-OCH_3-C_6H_4	H	$C_{11}H_8O_4N_2Br_2$	166 [b]	76	23.39 (23.11)	2.79 (1.40)	4.97 (4.90
3k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{18}H_{14}O_4N_2Br_2$	270 [b]	69	31.98 (31.95)	2.93 (2.07)	4.37 (4.14)

a = Compounds crystallized from aq methanol.

b = Compounds crystallized from glacial acetic acid.

c = Compounds crystallized from benzene.

Table III Characterization data of 2, 3-(3/- Hydroxyl benz)-1, 4-dioxo-7, 9-diaza-/ 7-aryl-7, 9-diaza-/ 7, 9-diaryl-7, 9-diaza-spiro [4, 5] deca-6, 8, 10-triones 1a-k

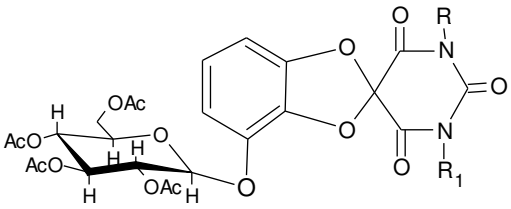


1a-k

Product	R	R_1	Formula	Mol.M.P. (^{0}C)	Yield (%)	% found(Calcd) C	H	N
1a	H	H	$C_{10}H_6O_6N_2$	180 [a]	80	48.12 (48.01)	2.23 (2.42)	11.44 (11.20)
1b	C_6H_5	H	$C_{16}H_{10}O_6N_2$	170 [a]	81	58.95 (58.90)	3.12 (3.09)	8.48 (8.59)
1c	C_6H_5	C_6H_5	$C_{22}H_{14}O_6N_2$	191 [a]	79	65.94 (65.67)	3.55 (3.51)	9.82 (9.96)
1d	*O*-CH_3-C_6H_4	H	$C_{17}H_{12}O_6N_2$	222 [a]	82	60.12 (60.00)	3.66 (3.55)	8.12 (8.23)
1e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{24}H_{18}O_6N_2$	212 [a]	78	66.67 (66.97)	4.72 (4.22)	6.91 (6.51)
1f	*p*-CH_3-C_6H_4	H	$C_{17}H_{12}O_6N_2$	125 [a]	81	60.12 (60.00)	3.77 (3.55)	8.18 (8.23)
1g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{24}H_{18}O_6N_2$	245 [a]	78	66.67 (66.97)	4.57 (4.22)	6.34 (6.51)
1h	*O*-OCH_3-C_6H_4	H	$C_{17}H_{12}O_7N_2$	165 [a]	80	57.53 (57.31)	3.33 (3.39)	7.98 (7.86)
1i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{24}H_{18}O_8N_2$	134 [a]	81	55.64 (62.34)	3.87 (3.92)	6.14 (6.06)
1j	*P*-OCH_3-C_6H_4	H	$C_{17}H_{12}O_7N_2$	196 [a]	76	57.53 (57.31)	3.31 (3.39)	7.96 (7.86)
1k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{24}H_{18}O_8N_2$	242 [a]	82	55.64 (62.34)	3.87 (3.92)	6.14 (6.06)

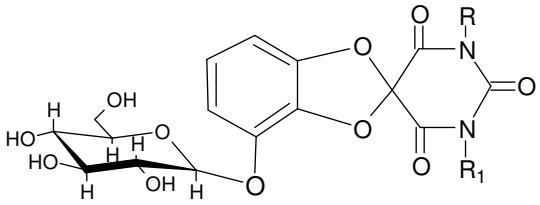
a = Compounds crystallized from glacial acetic acid.

Table IV Characterisation data of 2, 3-(3/-N-β-D-2, 3, 4, 6-tetra-*O*-acetyl-glucopyranose)-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones 2a-k



Product	R	R_1	Mol. Formula	Yield (%)	$[\alpha]^{29}_D$ (0)	% found(Calcd) C	H	N
2a	H	H	$C_{21}H_{27}O_{15}N_2$	64	52.72 (60.43)	60.15 (6.71)	6.73 (6.47)	6.42
2b	C_6H_5	H	$C_{27}H_{31}O_{15}N_2$	60	60.71	65.98 (65.72)	6.87 (6.68)	5.38 (5.67)
2c	C_6H_5	C_6H_5	$C_{33}H_{35}O_{15}N_2$	62	67.72	69.21 (69.59)	6.37 (6.15)	4.69 (4.92)
2d	*O*-CH_3-C_6H_4	H	$C_{28}H_{33}O_{15}N_2$	58	100.24	66.64 (66.27)	6.96 (6.50)	5.85 (5.52)
2e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{35}H_{39}O_{15}N_2$	62	113.48	70.69 (70.35)	6.84 (6.53)	4.91 (4.69)
2f	*p*-CH_3-C_6H_4	H	$C_{28}H_{33}O_{15}N_2$	61	-91.72	66.62 (66.27)	6.94 (6.50)	5.83 (5.52)
2g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{35}H_{39}O_{15}N_2$	65	72.47	70.67 (70.35)	6.87 (6.53)	4.93 (4.69)
2h	*O*-OCH_3-C_6H_4	H	$C_{28}H_{33}O_{16}N_2$	57	6.29	64.10 (64.24)	6.09 (6.30)	5.17 (5.35)
2i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{35}H_{39}O_{17}N_2$	64	35.85	66.93 (66.77)	6.53 (6.20)	4.76 (4.45)
2j	*P*-OCH_3-C_6H_4	H	$C_{28}H_{33}O_{16}N_2$	63	129.68	64.08 (64.24)	6.11 (6.30)	5.13 (5.35)
2k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{35}H_{39}O_{17}N_2$	59	112.34	66.52 (66.77)	6.03 (6.20)	4.83 (4.45)

Table V Characterisation data of 2, 3-(3′-N-β-D-2, 3, 4, 6-tetra-*O*-acetyl-glucopyranose)-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones 2a-k



Product	R	R_1	Mol. Formula	Yield (%)	$[\alpha]^{29}_D$ (^{0})	% found(Calcd) C	H	N
3a	H	H	$C_{16}H_{16}O_{11}N_2$	64	41.33	46.53 (46.61)	3.73 (3.91)	6.42 (6.79)
3b	C_6H_5	H	$C_{22}H_{20}O_{11}N_2$	60	59.37	54.02 (54.10)	4.08 (4.13)	5.58 (5.74)
3c	C_6H_5	C_6H_5	$C_{28}H_{24}O_{11}N_2$	62	63.32	59.43 (59.58)	4.37 (4.29)	4.69 (4.96)
3d	*O*-CH_3-C_6H_4	H	$C_{23}H_{22}O_{11}N_2$	58	100.67	54.62 (54.98)	4.28 (4.41)	5.43 (5.58)
3e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{30}H_{28}O_{11}N_2$	62	119.38	60.69 (60.81)	4.84 (4.76)	4.53 (4.73)
3f	*p*-CH_3-C_6H_4	H	$C_{23}H_{22}O_{11}N_2$	61	-95.72	54.62 (54.98)	4.28 (4.41)	5.43 (5.58)
3g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{30}H_{28}O_{11}N_2$	65	72.47	60.69 (60.81)	4.84 (4.76)	4.53 (4.73)
3h	*O*-OCH_3-C_6H_4	H	$C_{23}H_{22}O_{12}N_2$	57	83.21	53.10 (53.29)	4.16 (4.28)	5.17 (5.40)
3i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{30}H_{28}O_{13}N_2$	64	35.85	57.52 (57.69)	4.03 (4.52)	4.83 (4.49)
3j	*P*-OCH_3-C_6H_4	H	$C_{23}H_{22}O_{12}N_2$	63	129.68	53.10 (53.29)	4.16 (4.28)	5.13 (5.40)
3k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{30}H_{28}O_{13}N_2$	59	90.34	57.52 (57.69)	4.03 (4.52)	4.83 (4.49)

Table VI. Data for in vitro antibacterial and antifungal activities of compounds 6a-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.

Norfloxacine 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.

Conclusion:

In continuation of our work the synthesis such spiro system containing all mention moieties in which the synthesis of 2, 3- (4/- Hydroxyl benz)-1, 4-dioxo-7, 9-diaza [4, 5] deca-6, 8, 10-triones **4** based on the interaction of Pyrogallol and 5,5-dibromo barbituric acid,[13] . The interaction of potassium salt of **4 a** and acetobromoglucose (ACBG) afforded 2, 3-(3/-(2, 3, 4, 6-Tetra-*O*-acetyl-*O*-β-D-glucopyranosyloxybenz))-1, 4-dioxo-7, 9-diaza-spiro[4,5] deca-6, 8, 10-triones **5** which was finally deacetylated using sodium methoxide in methanol to gives 2, 3-(3/-*O*-β-D-Glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5] deca-6, 8, 10-triones **6** and herein we report the synthesis screening results of 2, 3-(3/-*O*-β-D-Glucopyranosyloxybenz)-1, 4-dioxo-7, 9-diaza-spiro[4, 5] deca-6, 8, 10-triones **6** inantibacterial and antifungal assays.

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