SYNTHESIS OF SPIRO BARBITURATES TRIONES AND GLYCOSIDES

P. K. GAIDHANE*, M. K. GAIDHANE, # , S. K. KHARKATE##
* Department of Chemistry, GWCOET, Nagpur, India
# Department of Chemistry , Shri Lemdeo Patil Mahavidhyalaya, Mandal, Nagpur, India
##Department of Chemistry, TGPCET, Nagpur, India
E-mail: Pravin.kg@rediffmail.com

Abstract
Malonic acid undergoes condensation readily with ureas to yield barbituric acids **2** which on bromination give 5,5-dibromobarbituric acids **3**. Reaction of glycerol with these 5,5-dibromo barbituric acids afforded 3-Hydroxymethyl-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 **4** which are on glucosylation gives 3-O-β-D-glucopyranosyl-oxy-methyl-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 **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, , dioxolane, triones, glucosides.

1. INTRODUCTION

Spiro compounds were prepared by many workers in search of different therapeutic properties 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-Dioxolanes have been used as antispasmodics,[7] sedatives, analgesic, tranquilizer and anesthesia.[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 3-O-β-D-Glucopyranosyloxymethyl-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones, herein we report the synthesis and screening results of 3-O-β-D-Glucopyranosyloxymethyl-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones in antibacterial and antifungal assays.

2. EXPERIMENTAL

2.1. 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 **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, 0.01mol) in H_2O (60 mL) at 50^{0}C. mp 235^{0}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 (Table **2**).

3-Hydroxymethyl-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-trione 4a: A mixture of 5,5-dibromo barbituric acid (2.85 g, 0.01mol), glycerol (1.41 g, 0.01mol), pyridine (0.79 g, 0.01 mol) and alcohol (25 mL) was refluxed for 3 hours. The

solvent was distilled off and the syrup poured on to crushed ice. The yellow solid was obtained. It was washed with alcohol, filtered and dried, yield (80 %). The compound was crystallized from glacial acetic acid, mp 240 ^{0}C. : IR (KBr) 3126 (strech. –OH), 3001 (NH), 1744 (C=O), 1233 (C-O-C), 1138 cm^{-1} (C-N-C) groups; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): 10 (H, NH), 3.9 (H, CH) and 3.5 (H, CH_2) and 2.0 ppm (H, OH)

Likewise, other substituted 3-hydroxymethyl-1, 4-dioxo-7, 9-diaza-spiro[4,5]deca-6, 8, 10-triones **4a-k** were prepared (Table-**3)**.

2, 3, 4, 6-Tetra-*O*-acetyl-α-D-glucopyranosylbromide or Acetobromoglucose (ACBG): The finely powered glucose pentaacetate (21.6 g) was added gradually to brominating agent. After the addition, the contents of flasks were allowed to stand at room temperature for 2-hours. The reaction mixture was then mixed with chloroform (30 mL) and the mixture was shaken vigorously for about 15 minutes. The resultant mixture was poured in to ice cold water. The chloroform layer was then separated. It was washed several times with aq $NaHCO_3$ to removed excess of perchloric acid followed by aq sodium metabisulphite to remove excess of bromine and finally 2-3 times with water. The $CHCl_3$ layer was then dried over anhydrous calcium chloride. The solvent was removed through vacuum distillation. The viscous oily liquid obtained after distillation was triturated several times with petroleum ether affords 2, 3, 4, 6-tetra-*O*-acetyl-α-D-glucopyranosylbromide as solid. It was crystallized from diethyl ether, (15 g) mp 88^{0}C.

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-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** (1.20 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-glucopyranosyloxymethyl)-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 59.66^0. : The product gave satisfactory elemental analyses and indicates its molecular formula.$C_{21}H_{27}N_2O_{15}$.

On the basis of all above facts, the products **5a** was assigned the structure as 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 (Table-**6**).

Likewise, various substituted 3-(2, 3, 4, 6-tetra-*O*-acetyl-*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 **5b-k** were prepared (Table-**4**).

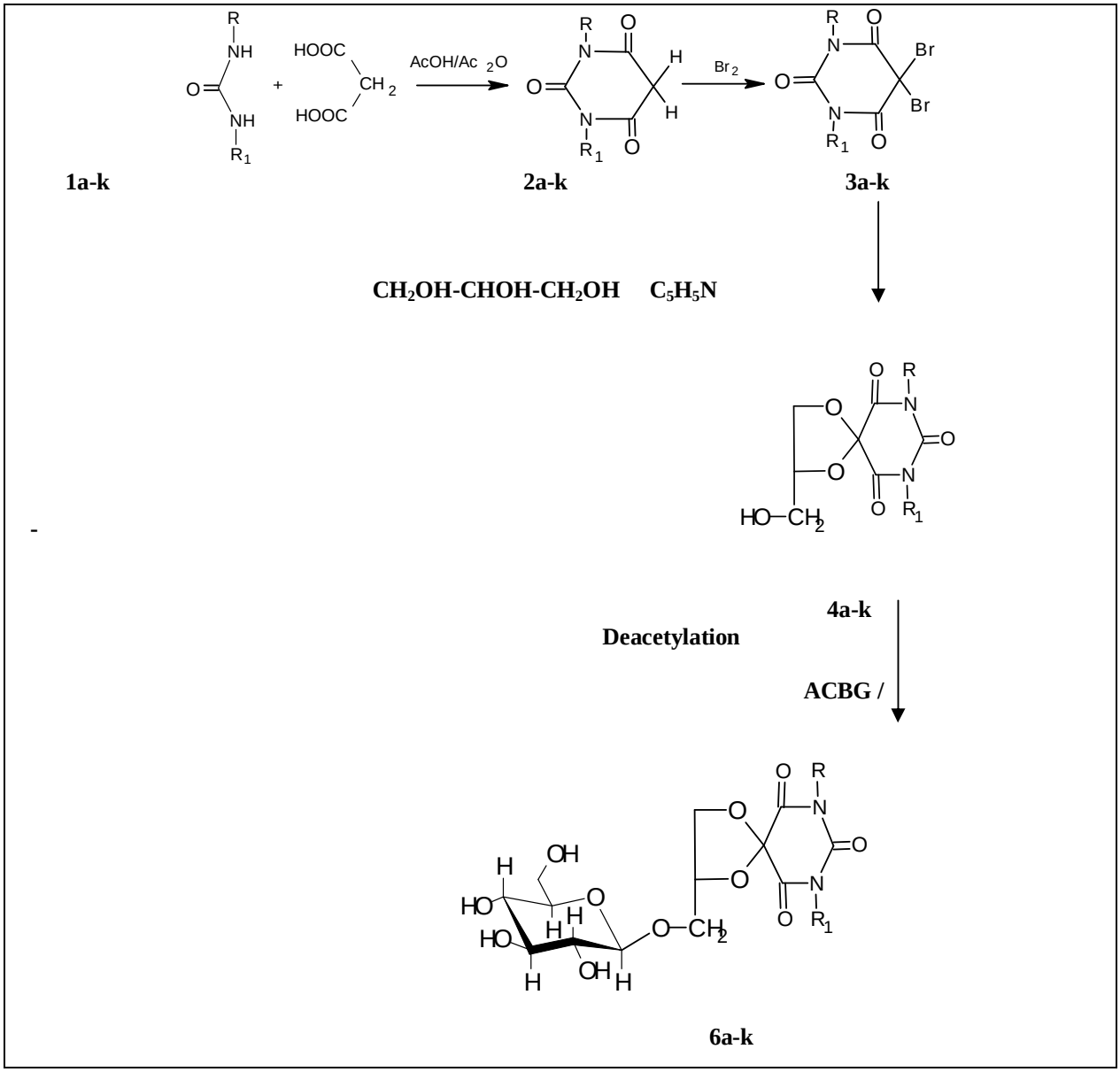
3-(O-β-D-Glucopyranosyloxymethyl)-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-trione 6a: A mixture of 3-(2, 3, 4, 6-tetra-O-acetyl-O-β-D-glucopyranosyloxymethyl)-1, 4-dioxo-7, 9-diaza-spiro[4,5]deca-6, 8, 10-triones **5a** (2.7 g), 5% sodium methoxide (20 mL) and methanol (30 mL) was stirred at room 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 (R*f* = 0.15), it was neutralized with ion-exchange resin (Amberlite IR 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 (56%). The compound was found to be optically active and its specific rotation $[\alpha]_D^{29}$ in methanol was found to be 48.13^0. IR (KBr) 3351 (glucosidic OH,) 3244 (NH), 1638 (C=O), 1310 (C-O-C) and 1154 cm^{-1} (C-N-C) groups ; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): 10. 1 (H, N-H), 3.73-5.03 (H, glucosidic CH), 3.5 (H, CH_2) and 2.0 ppm (H, glucosidic OH) ; EI MS[156-161]: 378 (M^+) and was dominated by m/z 216 ($C_{13}H_{18}N_2O_{11}$) with the loss of an intact sugar moiety, $C_6H_{10}O_6$. It also showed the molecular ion peak at m/z 199, 185, 72, and 60.

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-**5**).

3. 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, The reaction of 5,5-dibromo barbituric acid **3a** with glycerol afforded **4a**. IR spectrum of **4a** showed characteristic bands at 3126 (strech. –OH), 3001 (NH), 1744 (C=O), 1233 (C-O-C), 1138 cm^{-1} (C-N-C) groups and ^{1}H NMR spectrum showed signals at δ 10 (H, NH), 3.9 (H, CH) and 3.5 (H, CH_2) and 2.0

ppm (H, OH). The negative test for bromine, the absence of C-Br absorption band in the spectrum and the presence of strong band at 1233 cm^{-1} for C-O-C is fully consistent with structure of 3-hydroxymethyl-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones **4a.**



	R	R_1		R	R
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-I

The interaction of potassium salt of **4a** and acetobromoglucose (ACBG) afforded 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** in moderate yield. Finally **5a** was deacetylated using sodium methoxide in methanol to gives 3-O-β-D-Glucopyranosyloxymethyl-1, 4-dioxo-7, 9-diaza-spiro[4, 5]deca-6, 8, 10-triones **6a.** : IR spectrum of

6a showed characteristic bands at 3351 (glucosidic OH,) 3244 (NH), 1638 (C=O), 1310 (C-O-C) and 1154 cm^{-1} (C-N-C) groups. The ^1H NMR spectrum displayed signals at δ 10. 1 (H, N-H), 3.73-5.03 (H, glucosidic CH), 3.5 (H, CH_2) and 2.0 ppm (H, glucosidic OH). EI-Mass spectrum showed a molecular ion peak at 378 (M^+) and was dominated by m/z 216 ($C_{13}H_{18}N_2O_{11}$) with the loss of an intact sugar moiety, $C_6H_{10}O_6$. It also showed the molecular ion peak at m/z 199, 185, 72, and 60. All the compounds gave satisfactory C, H, and N elemental analysis.

3.1. MICROBIAL ACTIVITY

3.1.1. 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 37^0C 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 3).

3.1.2. 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 37^0C. 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).

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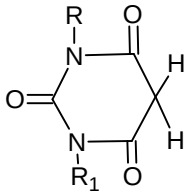
Table 1 Characterization data barbiturc acid and 1-aryl-/ 1,3-diaryl barbituric acids 2a-k

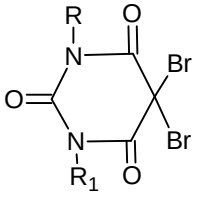


Product	R	R_1	Mol. Formula	M.P. (^{0}C)	Yield (%)	found(Calcd) % C	H	N
2a	H	H	$C_4H_4O_3N_2$	255 [a]	50	37.82 (37.50)	3.83 (3.12)	21.98 (21.87)
2b	C_6H_5	H	$C_{10}H_8O_3N_2$	262 [b]	48	59.69 (59.40)	3.98 (3.96)	13.93 (13.86)
2c	C_6H_5	C_6H_5	$C_{16}H_{12}O_3N_2$	238 [b]	52	69.23 (69.06)	4.54 (4.31)	10.37 (10.07)
2d	*O*-CH_3-C_6H_4	H	$C_{11}H_{10}O_3N_2$	181 [b]	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 [b]	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 [b]	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[c]	49	44.93	3.77	5.85
					(44.62)	(3.30)	(5.78)	
2h	*O*-OCH_3-C_6H_4	H	$C_{11}H_{10}O_4N_2$	253 [b]	41	32.42	2.76	6.97
					(32.11)	(2.43)	(6.81)	
2i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{18}H_{16}O_5N_2$	186 [b]	43	41.96	3.42	5.84
					(41.86)	(3.10)	(5.42)	
2j	*P*-OCH_3-C_6H_4	H	$C_{11}H_{10}O_4N_2$	190 [c]	49	32.47	2.81	6.96
					(32.11)	(2.43)	(6.81)	
2k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{18}H_{16}O_5N_2$	220 [b]	48	41.93	2.81	5.79
							(41.86)	
(3.10)	(5.42)							

a = Compounds crystallized from water.
b = Compounds crystallized from glacial acetic acid.
c = Compounds crystallized from ethanol.

Table 2 Characterization data 5,5-dibromobarbituric acid and 1-aryl-/ 1,3-diaryl-5,5-dibromo barbituric acids 3a-k

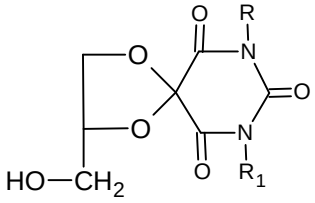


Product	R	R_1	Mol. Formula	M.P. (^{0}C)	Yield (%)	% found(Calcd) C	H	N
3a	H	H	$C_4H_2O_3N_2Br_2$	235 [a]	70	16.91	1.03	9.97
					(16.78)	(0.69)	(9.79)	
3b	C_6H_5	H	$C_{10}H_6O_3N_2Br_2$	184[b]	68	33.54	1.89	7.93
					(33.14)	(1.65)	(7.73)	
3c	C_6H_5	C_6H_5	$C_{16}H_{10}O_3N_2Br_2$	152 [c]	71	43.97	2.59	6.74
					(43.83)	(2.28)	(6.39)	
3d	*O*-CH_3-C_6H_4	H	$C_{11}H_8O_3N_2Br_2$	174 [b]	69	23.89	1.79	5.39
					(23.78)	(1.44)	(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	2.41	4.67
					(32.54)	(2.17)	(4.34)	
3f	*p*-CH_3-C_6H_4	H	$C_{11}H_8O_3N_2Br_2$	105 [b]	69	23.87	1.81	5.42
					(23.78)	(1.44)	(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	2.43	4.66
					(32.54)	(2.17)	(4.34)	
3h	*O*-OCH_3-C_6H_4	H	$C_{11}H_8O_4N_2Br_2$	181[c]	74	23.37	1.73	4.98

						(23.11)	(1.40)	(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	2.37	4.34
					(31.95)	(2.07)	(4.14)		
3j	*P*-OCH_3-C_6H_4	H	$C_{11}H_8O_4N_2Br_2$	166 [b]		76	23.39	2.79	4.97
					(23.11)	(1.40)	(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	2.93	4.37
							(31.95)		
(2.07)	(4.14)								

a = Compounds crystallized from aq methanol.
b = Compounds crystallized from glacial acetic acid.
c = Compounds crystallized from benzene.

Table 3 Characterization data of 3-Hydroxymethyl-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

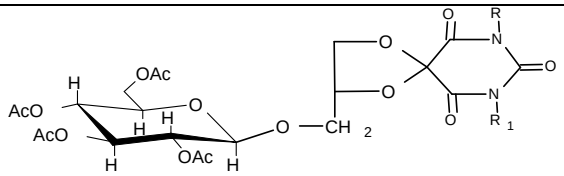


Product	R	R_1	Mol. Formula	M.P. (^{0}C)	Yield (%)	% found(Calcd) C	H	N
1a	H	H	$C_7H_8O_6N_2$	240 [a]	80	38.67	3.91	12.67
					(38.88)	(3.70)	(12.96)	
1b	C_6H_5	H	$C_{13}H_{12}O_6N_2$	164 [a]	82	53.77	4.43	9.87
					(53.42)	(4.10)	(9.58)	
1c	C_6H_5	C_6H_5	$C_{19}H_{16}O_6N_2$	192 [a]	79	61.63	4.11	7.93
					(61.95)	(4.34)	(7.60)	
1d	*O*-CH_3-C_6H_4	H	$C_{14}H_{14}O_6N_2$	218 [a]	82	54.66	4.85	9.49
					(54.90)	(4.57)	(9.15)	
1e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{21}H_{20}O_6N_2$	256 [a]	78	63.39	5.45	7.42
					(63.63)	(5.05)	(7.07)	
1f	*p*-CH_3-C_6H_4	H	$C_{14}H_{14}O_6N_2$	125 [a]	81	54.68	4.88	9.45
					(54.90)	(4.57)	(9.15)	
1g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{21}H_{20}O_6N_2$	235 [a]	79			
63.37	5.43	7.40						
					(63.63)	(5.05)	(7.07)	
1h	*O*-OCH_3-C_6H_4	H	$C_{14}H_{14}O_7N_2$	137 [a]	80	52.43	4.78	8.39

						(52.17)	(4.34)	(8.69)
1i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{21}H_{20}O_8N_2$	138 [a]		81	78.64	6.52 8.97
						(78.26)	(6.21)	(8.69)
1j	*P*-OCH_3-C_6H_4	H	$C_{14}H_{14}O_7N_2$	166 [a]		76	52.47	4.73 8.32
						(52.17)	(4.34)	(8.69)
1k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{21}H_{20}O_8N_2$	230 [a]		82	78.62	6.57 8.96
							(78.26)	(6.21) (8.69)

a = Compounds crystallized from glacial acetic acid.

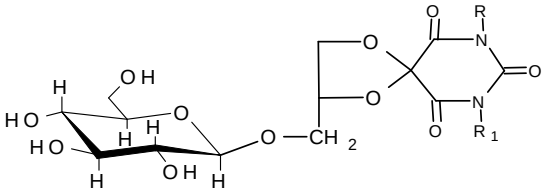
Table 4 Characterization data of 3-(2, 3, 4, 6-tetra-O-acetyl-O-β-D-glucopyranosyloxymethyl)-1, 4-dioxo-7, 9-diaza/ 7-aryl-7,9-diaza / 7,9-diaryl- 7,9-diaza-spiro[4,5]deca-6,8,10-triones **2a-k**



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	59.66	60.15	6.73	6.42
						(60.43)	(6.47)	(6.71)
2b	C_6H_5	H	$C_{27}H_{31}O_{15}N_2$	60	60.71	65.98	6.87	5.38
						(65.72)	(6.68)	(5.67)
2c	C_6H_5	C_6H_5	$C_{33}H_{35}O_{15}N_2$	62	67.72	69.21	6.37	4.69
						(69.59)	(6.15)	(4.92)
2d	*O*-CH_3-C_6H_4	H	$C_{28}H_{33}O_{15}N_2$	58	100.67	66.64	6.96	5.85
						(66.27)	(6.50)	(5.52)
2e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{35}H_{39}O_{15}N_2$	62	113.38	70.69	6.84	4.91
						(70.35)	(6.53)	(4.69)
2f	*p*-CH_3-C_6H_4	H	$C_{28}H_{33}O_{15}N_2$	61	-91.72	66.62	6.94	5.83
						(66.27)	(6.50)	(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	6.87	4.93
						(70.35)	(6.53)	(4.69)
2h	*O*-OCH_3-C_6H_4	H	$C_{28}H_{33}O_{16}N_2$	57	19.79	64.10	6.09	5.17
						(64.24)	(6.30)	(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	6.53	4.76
						(66.77)	(6.20)	(4.45)
2j	*P*-OCH_3-C_6H_4	H	$C_{28}H_{33}O_{16}N_2$	63	129.68	64.08		

6.11	5.13							
							(64.24)	(6.30) (5.35)
2k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{35}H_{39}O_{17}N_2$	59	-83.34	66.52		
6.03	4.83							
							(66.77)	
(6.20)	(4.45)							

Table 5 Characterization data of 3-O-β-D-glucopyranosyl-oxy-methyl-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 3a-k



Product	R	R_1	Mol. Formula	Yield (%)	$[\alpha]^{29}_D$ (^{0})	% found(Calcd) C	H	N
3a	H	H	$C_{13}H_{18}O_{11}N_2$	64	48.13	41.09	4.84	7.75
						(41.26)	(4.76)	(7.40)
3b	C_6H_5	H	$C_{19}H_{22}O_{11}N_2$	60	46.31	50.95	4.52	648
						(50.52)	(4.84)	(6.16)
3c	C_6H_5	C_6H_5	$C_{25}H_{26}O_{11}N_2$	62	62.78	56.34	4.61	5.06
						(56.60)	(4.90)	(5.28)
3d	*O*-CH_3-C_6H_4	H	$C_{20}H_{24}O_{11}N_2$	58	98.67	51.68	5.35)	5.68
						(51.28)	(5.12)	(5.98)
3e	*O*-CH_3-C_6H_4	*O*-CH_3-C_6H_4	$C_{27}H_{30}O_{11}N_2$	54	108.42	58.32	5.14	5.37
						(58.06)	(5.37)	(5.01)
3f	*p*-CH_3-C_6H_4	H	$C_{20}H_{24}O_{11}N_2$	63	-96.83	51.69	5.38)	5.66
						(51.28)	(5.12)	(5.98)
3g	*p*-CH_3-C_6H_4	*p*-CH_3-C_6H_4	$C_{27}H_{30}O_{11}N_2$	65	67.33	58.29		5.18 5.32
						(58.06)	(5.37)	(5.01)
3h	*O*-OCH_3-C_6H_4	H	$C_{20}H_{24}O_{12}N_2$	61	16.29	49.41	4.71	5.93
						(49.58)	(4.95)	(5.78)
3i	*O*-OCH_3-C_6H_4	*O*-OCH_3-C_6H_4	$C_{27}H_{30}O_{13}N_2$	57	33.85	59.65	5.27	4.90
						(59.91)	(5.08)	

(4.74)							
3j	*P*-OCH_3-C_6H_4	H	$C_{20}H_{24}O_{12}N_2$	62	133.68	49.39	4.74
5.96							
						(49.58)	(4.95)
(5.78)							
3k	*P*-OCH_3-C_6H_4	*P*-OCH_3-C_6H_4	$C_{27}H_{30}O_{13}N_2$	64	-74.34	59.63	
5.24	4.92						
						(59.91)	(5.08)
(4.74)							

Table 6. 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.
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.

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