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Carbs-Derived Spiro barbiturates And Their Biological Activities

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ABSTRACT:

*By using Biltz and Wittek method, the Malonic acid condensed readily with ureas-**1** to yield barbituric acids **2** which on bromination give 5,5-dibromobarbituric acids **3**. On the reaction of compound **3** with α-D-glucose (sheme-1) and α-D-galactose (scheme-2) afforded 2,3-α-D-glucopyrano-1,4-dioxo-7,9-diaza-spiro[4, 5]deca-6,8,10-triones **4a** and 2, 3-α-D-galactopyrano-1, 4-dioxo-7, 9-diaza-spiro[4,5]deca-6,8,10-triones **4a** respectively. 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, α-D-glucose, α-D-galactose, dioxolane, barbiturates, spirotriones.

INTRODUCTION:

Carbohydrates or carbs are sugar molecules involved in almost every aspect of living organisms and perform various important biological functions. The naturally occurring carbohydrates and their derivatives have been extensively studied as therapeutic agents for the treatment of various diseases. Drugs with carbohydrate moieties have been approved as diagnostic agents. Glucose, galactose and fructose all have the same chemical formula ($C_6H_{12}O_6$), they differ structurally and chemically because of the different arrangement of functional groups around the asymmetric carbon; all of these monosaccharides are carbohydrates. Carbohydrates increase the water and lipid solubility of the pharmacophoric group and exhibit a variety of biological and therapeutic properties. Certain glycoconjugates and galactoconjugates are more readily excretable and resistant to significant metabolic transformation.[1-3] 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, sedatives, analgesic, tranquilizer and anesthesia.[7-8] Spiro systems have unique structural and reactivity pattern. Many spiro compounds possess antiparasitic and analgesic activities. 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, some Spirocarbocyclic systems also enhance biological potency of compounds. [9-12]

In continuation of our work on the synthesis and biological activities of spirobarbiturates[13,14], biological activities of spiro system, 1,3-dioxolane and importance of carbs moieties, herein we report the synthesis of 2, 3-α-D-glucopyrano-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 (scheme-1)** and 2, 3-α-D-galactopyrano-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 (scheme-2)** and showed the screening results in antibacterial and antifungal assays.

2. RESULTS AND DISCUSSION

Biltz and Wittek method[15-16] is used to reared barbituric acids **2** by condensing urea 1 with malonic acid in presence of acetic acid-acetic anhydride. Then by adding bromine to barbituric acids in suitable solvents get 5, 5-Dibromo barbituric acids **3** [17-18]. 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. In present scheme (1 and 2), the rate of the 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 10 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-glucopyranose afforded glucocojugated spirotrioes **4a (**Scheme-1) and similarly compound **3a** on reaction with α-D-galactopyranose offered galacto- cojugated spirotrioes **4a (**Scheme-1). Both spirotriones gave 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 are fully consistent with structure of 2, 3-α-D-glucopyrano-1, 4-dioxo-7, 9- diaza- spiro [4,5]deca-6,8,10-triones **4a** (scheme-1) and 2,3-α-D-galactopyrano-1,4-dioxo-7,9- diaza- spiro [4,5]deca-6,8,10-triones **4a** (scheme-2)**.** In case of scheme-1, the compound **4a** showed IR spectrum characteristic bands at 3131 (OH), 3061 (NH), 2956 (glucosidic CH), 1707 (C=O), 1263 1176 cm^{-1} (C-N-C) and 1152 (-CO) groups. The ^{1}H NMR spectrum of **4a** showed signals at δ 10 (s, 1H, N-H), 3.79, (H, CH_2) 9.79 (s, 1H, OH) and 3.76-3.40 ppm (H, glucosidic CH). In the proton-decoupled ^{13}C NMR, the anomeric carbon C-1' and C-2' resonated at 103 and 84 ppm respectively. In the case of **scheme-2,** product **4a** showed IR spectrum characteristic bands at 3131 (OH), 3061 (NH), 2956 (galactosidic CH), 1707 (C=O), 1263 1176 cm^{-1} (C-N-C), and 1152 (-CO) groups. The ^{1}H NMR spectrum of **4a** showed signals at δ 10 (s, 1H, N-H), 3.79, (H, CH_2) 9.79, (s, 1H, OH) and 3.76-3.40 ppm (H, galactosidic CH). In ^{13}C NMR, the anomeric carbon C-1' and C-2' resonated at 103 and 84 ppm respectively. The ES-MS spectrum of compound 4a of scheme-1 and scheme-2 showed a molecular ion peak at 304 (M^+) and dominated by m/z 126 ($C_4O_3N_2H_2$) with the loss of 178 amu corresponding to the loss of 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. From the screening result, it was found that water solubility of compound 2, 3-α-D-glucoconjugates **(4a-k)** and 2, 3-α-D-galactoconjugates- **(4a-K)** increases and also exhibit a variety of microbial activity.

2.1. MICROBIAL ACTIVITY

2.1.1. Antimicrobial activity

The synthesized compounds **(4a-k)** of both scheme-1 and scheme-2 were screened for their antibacterial and 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. The same procedure was adopted for pure Norfloxacine and the corresponding zone diameters were compared. The screening results indicate that 2, 3-α-D-glucopyrano-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 (scheme-1)** and 2, 3-α-D-galactopyrano-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 (scheme-2)** showed moderate to excellent bactericidal activities against both organisms **(Table 6).**

2.1.2. Antifungal activity

The antifungal activity of synthesized compound 4a of both scheme-1and scheme-2 were evaluated by the using the 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 Gentamycin was also tested under similar condition with a view of comparing the results. The compounds 2,3-α-D-gluco- conjugated spiro-triones **(4a-k)** and 2, 3-α-D-galactoconjugated spiro-triones **4a-k** (Scheme 1 and 2 respectively) showed significant fungitoxicity against both the test fungi **(Table 7).**

3. EXPERIMENTAL

3.1. General methods

Substituted ureas 1 were prepared as described in the literature **(Table-1).**[19] Melting points were determined in open glass capillaries and are uncorrected. Optical rotations were measured at 29^0C. Elemental analysis ware determined by using the Perkin Elmer 2400 CHN analyzer. FT-IR spectra were recorded by 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 by 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 65^0C and 4 mL of acetic anhydride was added during 30 min. The reaction mixture was heated with stirring at 90^0C for 3 h. The solvent was removed by distillation under vacuum at 60^0C 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 255^0C (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 2).**

5,5-Dibromobarbituric acid 3a. This was prepared by adding molecular bromine (2.55 g, 0.016 mol) to barbituric acids **2a**

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

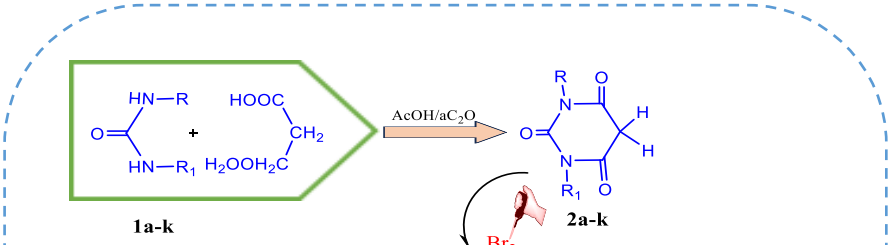
2,3-α-D-Glucopyrano-1,4-dioxo-7,9-diaza-spiro[4,5]deca-6,8,10-triones 4a. (Scheme-1):

A mixture of 5,5-dibromo barbituric acid **3a** (2.85 g, 0.01mol), α-D-glucose (1.80 g, 0.01mol), pyridine (0.79 g, 0.01 mol) and alcohol (25 mL) were refluxed for 3 hour. The excess of solvent was distilled off and the syrup poured on to crushed ice to obtain **4a**. The compound was filtered, washed with alcohol and dried under reduced pressure. The compound **4a** was crystallized from glacial acetic acid, mp >285 ^{0}C (Yield 80 %); Elemental analysis (Found: C, 39.71; H, 3.81; N, 7.34 %. $C_{10}O_9N_2H_{12}$ requires C, 39.47; H, 3.94; N, 7.36%). *vmax* (KBr)/cm^{-1} 3131(-OH), 3061 (-NH), 2956 (glucosidic-CH), 1708 (C=O), 1263 (C-O-C), 1176 (C-N-C), 1152 (C-O). *λmax*/nm (ξ/M^{-1} cm^{-1}) (300 MHz, $CDCl_3$+DMSO-d_6) δ_H 10 (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). δ_C 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'); EI-MS: m/z 304 (M^+, $C_{10}O_9N_2H_{12}$) and 126 ($C_4O_3N_2H_2$). When the reaction of α-D-glucopyranose was extended with several other 5,5-dibromo-1-aryl-and 1,3-diaryl barbituric acids **(3b-k),** then corresponding 2,3-α-D-glucopyrano-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 **(4b-k)** have been synthesized.

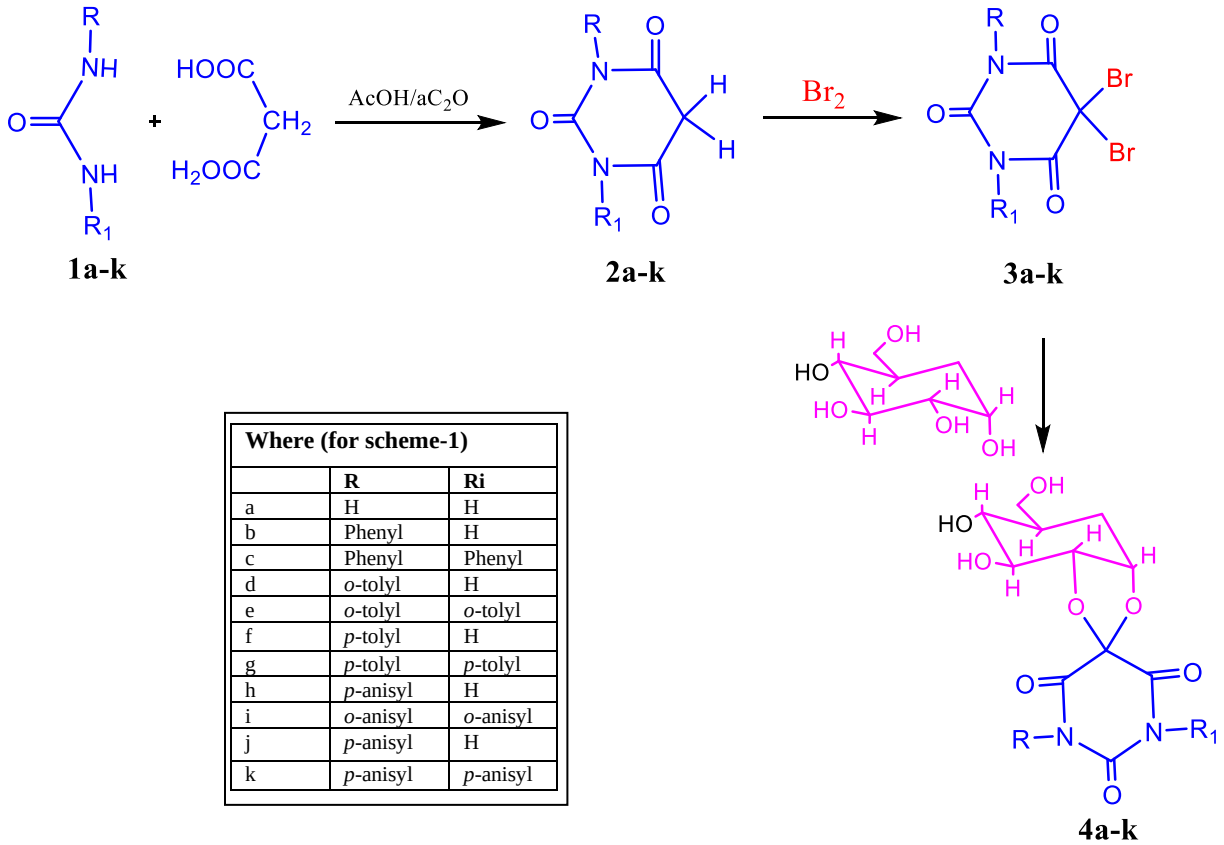
2,3-α-D-Galactopyrano-1, 4-dioxo-7, 9-diaza-spiro[4,5]deca-6,8,10-triones 4a. (Scheme-2):

A mixture of 5,5-dibromo barbituric acid **3a** (2.85 g, 0.01mol), α-D-galactose (1.80 g, 0.01mol), pyridine (0.79 g, 0.01 mol) and alcohol (25 mL) were refluxed for 3 hour. The excess of solvent was distilled off and the syrup poured on to crushed ice to obtain **4a.** The compound was filtered, washed with alcohol and dried under reduced pressure. The compound **4a** was crystallized from glacial acetic acid, mp >285 ^{0}C (AcOH) (Yield 79 %); Elemental analysis (Found: C, 39.71; H, 3.72; N, 7.44 % $C_{10}O_9N_2H_{12}$ requires C, 39.47; H, 3.94; N, 7.36 %). 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^+, $C_{10}O_9N_2H_{12}$) and 126 ($C_4O_3N_2H_2$);

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, 9-diaza/7-aryl-7,9-diaza/ 7,9-diaryl-7,9-diaza-spiro [4, 5] deca-6,8,10-triones **(4b-k)** have been synthesized.

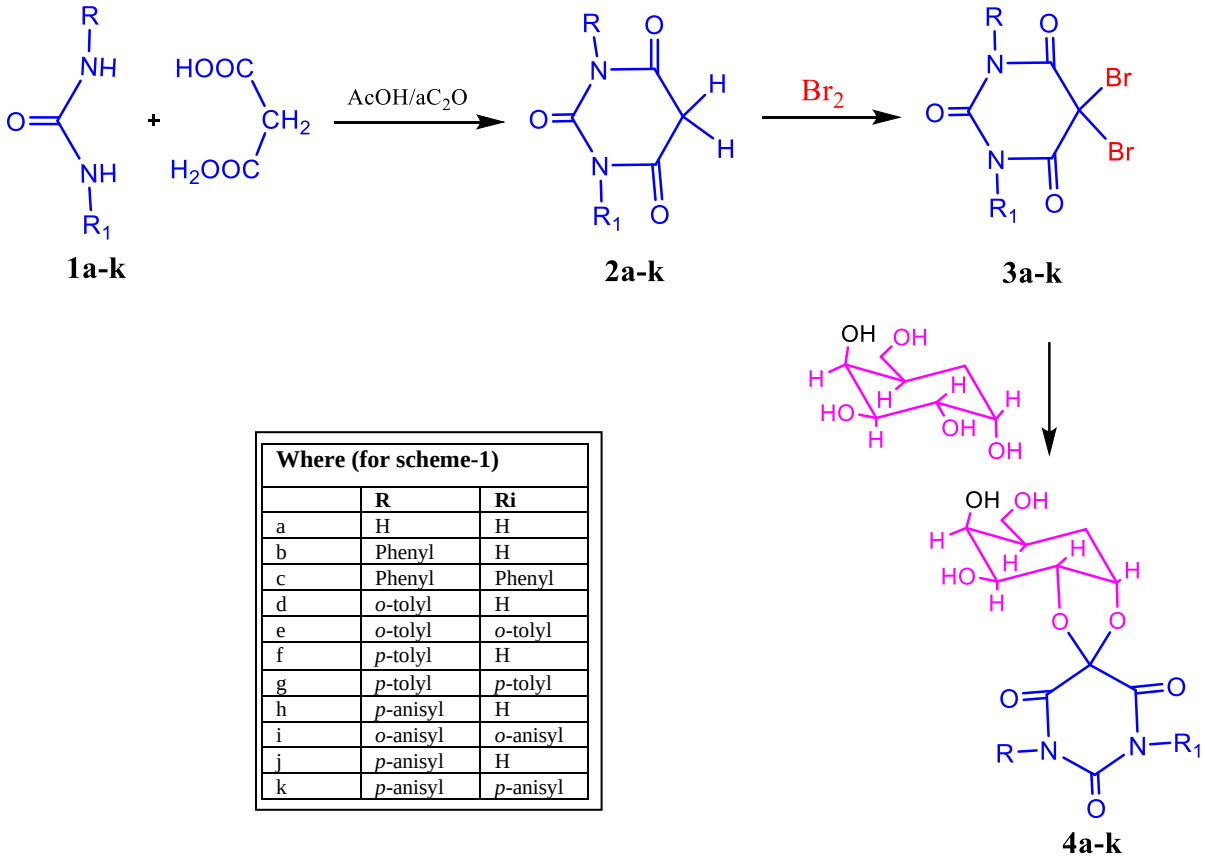


Scheme-1: 2,3-α-D-glucopyrano-1, 4-dioxo-7-aryl- 7, 9-diaza- and 7, 9-diaryl-7, 9-diaza-spiro[4, 5]deca-6,8,10-triones (4a-k).



Where (for scheme-1)		
	R	**Ri**
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-2: 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 (4a-k).



1a-k **2a-k** **3a-k** **4a-k**

Where (for scheme-1)		
	R	**Ri**
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

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

Product	R	R_1	Mol. Formula	M.P. (^{0}C)	Solvent used for crystalization
a	H	H	CH_4ON_2	132	--
b	Phenyl	H	$C_7H_6ON_2$	147[a]	Compound crystallized from water
c	Phenyl	Phenyl	$C_{13}H_{10}ON_2$	242[b]	Compound crystallized from glacial acetic acid
d	*o*-tolyl	H	$C_8H_8ON_2$	198[a]	Compound crystallized from water
e	*o*-tolyl	*o*-tolyl	$C_{15}H_{14}ON_2$	253[b]	Compound crystallized from glacial acetic acid
f	*p*-tolyl	H	$C_8H_8ON_2$	180[a]	Compound crystallized from water
g	*p*-tolyl	*p*-tolyl	$C_{15}H_{14}ON_2$	254[b]	Compound crystallized from glacial acetic acid
h	*p*-anisyl	H	$C_8H_8O_2N_2$	168[a]	Compound crystallized from water
i	*o*-anisyl	*o*-anisyl	$C_{15}H_{14}O_3N_2$	184[b]	Compound crystallized from glacial acetic acid
j	*p*-anisyl	H	$C_8H_8O_2N_2$	168[a]	Compound crystallized from water
k	*p*-anisyl	*p*-anisyl	$C_{15}H_{14}O_3N_2$	234[b]	Compound crystallized from glacial acetic acid

Table 2: 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	C	H	N
a	H	H	$C_4H_4O_3N_2$	255[a]	50	37.82	03.83	21.98	(37.50)	(03.12)	(21.87)
b	Phenyl	H	$C_{10}H_8O_3N_2$	262[b]	48	59.69	03.98	13.93	(59.40)	(03.96)	(13.86)
c	Phenyl	Phenyl	$C_{16}H_{12}O_3N_2$	238[b]	52	69.23	04.54	10.37	(69.06)	(04.31)	(10.07)
d	*o*-tolyl	H	$C_{11}H_{10}O_3N_2$	181[b]	44	33.69	02.84	07.39	(33.41)	(02.53)	(07.08)
e	*o*-tolyl	*o*-tolyl	$C_{18}H_{16}O_3N_2$	210[b]	47	44.91	03.72	05.86	(44.62)	(03.30)	(05.78)
f	*p*-tolyl	H	$C_{11}H_{10}O_3N_2$	243[b]	44	33.57	02.91	07.33	(33.41)	(02.53)	(07.08)
g	*p*-tolyl	*p*-tolyl	$C_{18}H_{16}O_3N_2$	233[c]	49	44.93	03.77	05.85	(44.62)	(03.30)	(05.78)
h	*p*-anisyl	H	$C_{11}H_{10}O_4N_2$	253[b]	41	32.42	02.76	06.97	(32.11)	(02.43)	(06.81)
i	*o*-anisyl	*o*-anisyl	$C_{18}H_{16}O_5N_2$	186[b]	43	41.96	03.42	05.84	(41.86)	(03.10)	(05.42)
j	*p*-anisyl	H	$C_{11}H_{10}O_4N_2$	190[c]	49	32.47	02.81	06.96	(32.11)	(02.43)	(06.81)
k	*p*-anisyl	*p*-anisyl	$C_{18}H_{16}O_5N_2$	220[b]	48	41.93	02.81	05.79	(41.86)	(03.10)	(05.42)

a	Crystallized from water	b	Crystallized from glacial acetic acid.	c	Crystallized from ethanal

Table 3: 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 C	H	N	% (calcd) C	H	N
a	H	H	$C_4H_2O_3N_2Br_2$	235 [a]	70	16.91	01.03	09.97	(16.78)	(00.69)	(09.79)
b	Phenyl	H	$C_{10}H_6O_3N_2Br_2$	184[b]	68	33.54	01.89	07.93	(33.14)	(01.65)	(07.73)
c	Phenyl	Phenyl	$C_{16}H_{10}O_3N_2Br_2$	152 [c]	71	43.97	02.59	06.74	(43.82)	(02.48)	(06.59)
d	*o*-tolyl	H	$C_{11}H_8O_3N_2Br_2$	174 [b]	69	23.89	01.79	05.39	(23.78)	(01.44)	(05.04)
e	*o*-tolyl	*o*-tolyl	$C_{18}H_{14}O_3N_2Br_2$	190 [a]	71	33.82	02.41	04.67	(32.54)	(02.17)	04.34)
f	*p*-tolyl	H	$C_{11}H_8O_3N_2Br_2$	105 [b]	69	23.87	01.81	05.42	(23.78)	(01.44)	(05.04)
g	*p*-tolyl	*p*-tolyl	$C_{18}H_{14}O_3N_2Br_2$	265 [b]	75	33.83	02.43	04.66	(32.54)	(02.17)	(04.34)
h	*p*-anisyl	H	$C_{11}H_8O_4N_2Br_2$	181[c]	74	23.37	01.73	04.98	(23.11)	(01.40)	(04.90)
i	*o*-anisyl	*o*-anisyl	$C_{18}H_{14}O_4N_2Br_2$	164 [b]	72	31.99	02.37	04.34	(31.95)	(02.07)	(04.14)
j	*p*-anisyl	H	$C_{11}H_8O_4N_2Br_2$	166 [b]	76	23.39	02.79	04.97	(23.11)	(01.40)	(04.90)
k	*p*-anisyl	*p*-anisyl	$C_{18}H_{14}O_4N_2Br_2$	270 [b]	69	31.98	02.93	04.37	(31.95)	(02.07)	(04.14)

a	Crystallized from aq methanol.	b	Crystallized from glacial acetic acid.	c	Crystallized from benzene

Table 4: Characterization data of 2,3-α-D-glucopyrano-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 (4a-k) (Scheme-1)

Product	R	R_1	Mol. Formula	Yield (%)	M.P. (ºC)	$[\alpha]^{29}_D$ (º)	% found C	H	N	% (calcd) C	H	N
a	H	H	$C_{10}H_{12}O_9N_2$	80	>285 [a]	51.72	39.69	03.81	07.36	(39.47)	(03.94)	(07.36)
b	Phenyl	H	$C_{10}H_{12}O_9N_2$	82	164 [a]	58.71	50.92	04.56	07.47	(50.52)	(04.21)	(07.36)
c	Phenyl	Phenyl	$C_{22}H_{20}O_9N_2$	79	198 [a]	62.72	57.92	04.59	06.37	(57.89)	(04.38)	(06.14)
d	*o*-tolyl	H	$C_{17}H_{17}O_9N_2$	82	228 [a]	102.67	51.75	04.66	07.12	(51.64)	(04.56)	(07.08)
e	*o*-tolyl	*o*-tolyl	$C_{24}H_{24}O_9N_2$	78	252 [a]	121.38	59.21	04.78	05.98	(59.50)	(40.95)	(05.78)
f	*p*-tolyl	H	$C_{17}H_{17}O_9N_2$	81	105 [a]	-97.72	51.72	04.73	07.10	(51.64)	(04.56)	(07.08)
g	*p*-tolyl	*p*-tolyl	$C_{24}H_{24}O_9N_2$	79	265 [a]	80.47	59.25	04.72	05.98	(59.50)	(04.95)	(05.78)
h	*p*-anisyl	H	$C_{17}H_{18}O_{10}N_2$	80	137 [a]	66.29	49.54	04.36	06.92	(49.75)	(04.14)	(06.82)
i	*o*-anisyl	*o*-anisyl	$C_{24}H_{24}O_{11}N_2$	81	118 [a]	35.85	55.61	04.94	05.72	(55.81)	(04.65)	(05.42)
j	*p*-anisyl	H	$C_{17}H_{18}O_{10}N_2$	76	166 [a]	129.68	49.54	04.32	06.92	(49.75)	(04.14)	(06.82)
k	*p*-anisyl	*p*-anisyl	$C_{24}H_{24}O_{11}N_2$	82	270 [a]	-58.34	55.61	04.83	05.79	(55.81)	(04.65)	(05.42)

a	**Synthesized compound (4a-k: Scheme-1) crystalized from glacial acetic acid**

Table 5: Characterization data of 2,3-α-D-galactopyrano-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 (4a-k). (Scheme-2)

Product	R	R_1	Mol. Formula	Yield (%)	M.P. (ºC)	$[\alpha]^{29}_D$ (º)	% found C	H	N	% (calcd) C	H	N
a	H	H	$C_{10}H_{12}O_9N_2$	79	>285 [a]	50.72	39.71	03.71	07.44	(39.47)	(03.94)	(07.36)
b	Phenyl	H	$C_{10}H_{12}O_9N_2$	81	170 [a]	60.71	50.95	04.52	07.48	(50.52)	(04.21)	(07.36)
c	Phenyl	Phenyl	$C_{22}H_{20}O_9N_2$	79	191 [a]	67.72	57.94	04.55	06.34	(57.89)	(04.38)	(06.14)

d	*o*-tolyl	H	$C_{17}H_{17}O_9N_2$	82	222 [a]	100.67	51.95	04.66	07.12	(51.64)	(04.56)	(07.08)
e	*o*-tolyl	*o*-tolyl	$C_{24}H_{24}O_9N_2$	78	212 [a]	113.38	59.18	0 4.72	05.91	(59.50)	(40.95)	(05.78)
f	*p*-tolyl	H	$C_{17}H_{17}O_9N_2$	81	125 [a]	-91.72	51.76	04.77	07.18	(51.64)	(04.56)	(07.08)
g	*p*-tolyl	*p*-tolyl	$C_{24}H_{24}O_9N_2$	79	245 [a]	72.47	59.22	04.77	05.90	(59.50)	(04.95)	(05.78)
h	*p*-anisyl	H	$C_{17}H_{18}O_{10}N_2$	80	165 [a]	46.29	49. 51	04.33	06.98	(49.75)	(04.14)	(06.82)
i	*o*-anisyl	*o*-anisyl	$C_{24}H_{24}O_{11}N_2$	81	134 [a]	35.85	55.62	0 4.90	05.77	(55.81)	(04.65)	(05.42)
j	*p*-anisyl	H	$C_{17}H_{18}O_{10}N_2$	76	196 [a]	129.68	49.53	04.31	06.96	(49.75)	(04.14)	(06.82)
k	*p*-anisyl	*p*-anisyl	$C_{24}H_{24}O_{11}N_2$	82	242 [a]	-54.34	55.64	04.87	05.76	(55.81)	(04.65)	(05.42)

a	**Synthesized compound (4a-k: Scheme-2) crystalized from glacial acetic acid**

Table 6. Data for in vitro antibacterial and antifungal activities of compounds 4a-k (Scheme-1) (Diameter of inhibition zone (in mm)

Product	Bacterial Strains		Fungal Strains	
	E coli	B. subtilis	A. niger	C. albicans
a	25	17	21	19
b	23	25	23	20
c	21	15	23	16
d	28	15	23	20
e	21	21	22	20
f	18	13	17	--
g	24	16	22	18
h	11	14	16	16
i	15	18	24	21
j	13	21	--	17
k	14	--	21	21

Result & Discussion: - - = no inhibition of growth.

Diameter of zone of inhibition from 22-28 (in mm) shows excellent activity, that of 16-21 (in mm) exhibits moderate activity and that of 11-15 (in mm) shows poor activity for bacterial strains.

Diameter of zone of inhibition from 20-24 (in mm) shows excellent activity, that of 15-19 (in mm) exhibits moderate activity and that of 11-14 (in mm) shows poor activity for Fungal Strains.

Table 7. Data for in vitro antibacterial and antifungal activities of compounds 4a-k (Scheme-2) (Diameter of inhibition zone (in mm)

Product	Bacterial Strains		Fungal Strains	
	E coli	B.subtilis	A. niger	C. albicans
a	15	19	21	23
b	14	16	17	15
c	10	09	11	--

d	12	10	15	23
e	16	14	24	28
f	13	13	17	--
g	14	16	22	18
h	11	14	16	16
i	15	13	23	21
j	13	11	--	17
k	14	16	22	22

Result & Discussion: - - = no inhibition of growth.

Diameter of zone of inhibition from 22-28 (in mm) shows excellent activity, that of 16-21 (in mm) exhibits moderate activity and that of 11-15 (in mm) shows poor activity for bacterial strains.

Diameter of zone of inhibition from 20-24 (in mm) shows excellent activity, that of 15-19 (in mm) exhibits moderate activity and that of 11-14 (in mm) shows poor activity for Fungal Strains.

Ciprofloxacine 100 µg/mL used as standard against E. *coli*, and *B. subtilis*, diameter of zone of inhibition is 35 and 29 respectively.

Gentamycine100 µg/mL used as standard against A. *niger* and *C. albicans*, diameter of zone of inhibition is 25 and 21 respectively.

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