FACILE SYNTHESIS OF BIOLOGICALLY ACTIVE LINEAR BISAROYL BENZODIFURANS BY PTC AND SOLVENT FREE MICROWAVE IRRADIATION

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Abstract

2,6-Diaroyl/naphthoyl-3,5-dialkyl/phenyl-benzo[1,2-b;5,4-b']difurans (**3a-e**, **4a-g** and **5a-g**) have been synthesized by condensing 4,6-diacyl/diaroyl resorcinols (**1 i-iii**) with various *p*-substituted α-bromoketones (**2a-g**) by (a) phase transfer catalysis method & (b) microwave irradiation. A comparison has been made between the two methods. Microwave irradiation has been found to be an efficient route for the synthesis of bisaroylbenzodifurans. All the compounds have been screened for anti-bacterial (**3a-e**, **4a-g** and **5b-g**) and some of the selected compounds have been tested for anti-implantation activity. The benzodifurans **3c**, **3d**, **3e**, **4a**, **4b**, **4d**, **4f** and **5g** have shown excellent activity against gram positive bacteria and the compound **4c** has shown 67% anti-implantation activity at 10 mg/Kg/rat/day on albino rats.

Introduction

The naturally occurring and synthetic benzofuran derivatives are known to be associated with biological and pharmacological activities. Methyl-2-methyl-5-hydroxy-6-acetyl-benzofuran-3-carboxylate (1), 2-ethyl-3-(3',5'-diiodo-4-hydroxybenzoyl)benzofuran (2) have been reported to exhibit anti-inflammatory, analgesic, anti-spasmodic and coronary vasodilatory properties. 2,6,8-trimethyl benzo[1,2-b; 5,4-b']difuran (3) is found to exhibit potent dermal photosensitizing activity.5-acetyl-6-cyanomethoxy-4-methoxybenzofuran,3-acetyl-2-amido-4-methoxydifurobenzene(4), and 2-nitro benzo[1,2-b; 5,4-b']difuran (5) were found active against gram positive and gram negative bacteria. 3-methyl-5-acetyl-6-hydroxybenzofuran (6), 2-(4-hydroxybenzoyl)benzofuran (7), 2-phenyl-3-[*p*-(β-diethylaminoethoxyphenyl)]-6-methoxybenzofuran (8) have shown potent anti-implantation activity. We have reported 100% anti-implantation activity of 2,6-dibenzoyl-3,5-dimethyl-benzo[1,2-b;5,4-b']difuran (9) (**3a**) at 2 mg/kg/rat/day on albino rats.

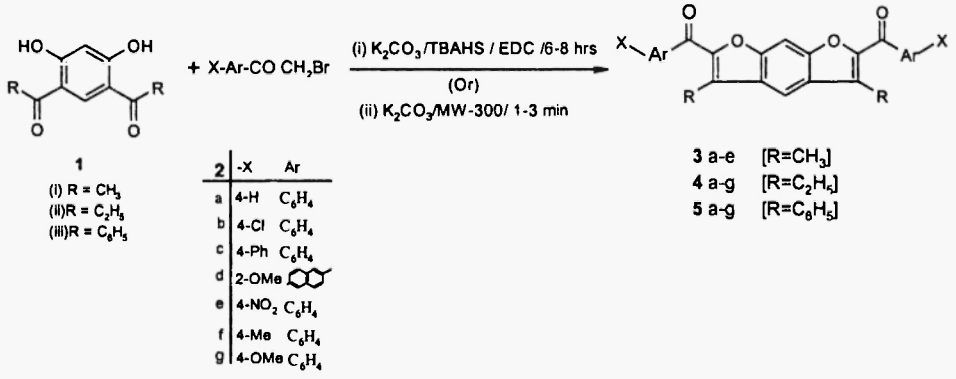
It is evident from the literature that, 2,6-diaroyl/naphthoyl-3,5-dialkyl/phenyl-benzo[1,2-b;5,4-b']difurans were not reported for anti-bacterial activity.

Encouraged by our earlier reported anti-implantation activity results of aroyl benzodifurans[6,9], we have designed the synthesis of bisaroylbenzodifurans (**3a-e**, **4a-g** , **5a-g**) with ethyl and phenyl substitutions at 3 and 5 positions, to evolve their anti-implantation and anti-bacterial activities. So in the present communication, we report an effective method of synthesis of 2,6-bis aroyl / naphthoyl-3,5-dialkyl/ phenyl benzodifurans.

We have reported the synthesis of 2,6-dibenzoyl-3,5-dimethyl-benzo[1,2-b;5,4-b']difurans under baked K_2CO_3 - anhydrous acetone method, and also under PTC condition (9). We have found that PTC method was an efficient method for the synthesis of bisaroyl benzodifuran.

In the present communication, we report the synthesis of 2,6-diaroyl /naphthoyl-3,5-di diethyl/phenyl-benzo[1,2-b;5,4-b'] difurans (**3a-e**, **4a-g** and **5a-g**) under phase transfer catalytic method, i.e., by condensing 4,6-dipropionyl / benzoyl resorcinol (10) (**1 i-iii**) with various *p*-substituted α-bromoketones (11-15) (**2a-g**) in presence of tetrabutyl ammonium hydrogen sulphate as a catalyst in ethylenedichloride for 6-8 hours at 55-60^0. This procedure avoids anhydrous conditions and long duration of reaction time.

There has been a growing interest in the use of microwave heating in organic synthesis. This has prompted us to synthesize the linear bisaroylbenzodifurans under microwave irradiation. In the present communication, we have adopted the microwave irradiation technique for the synthesis of bisaroylbenzodifurans under solvent free conditions for the first time. The 4,6-diacyl/aroyl resorcinols and the substituted α-bromoketones (**2a-g**) were doped with baked K_2CO_3 as a solid support, and the mixture was irradiated at 300W for a period of 1-3 minutes. After irradiation, the inorganic substances were removed and the resulting product was crystallized from methanol. The results were tabulated in **Table 2**. A comparison was also conducted between the two methods of synthesis (PTC and MW) from the available data (in **Table 2**). Microwave method is found to be convenient and simple. It does not require toxic solvents and the time of the reaction are also curtailed with reference to PTC method and the yields obtained from MW method are encouraging. The schematic representation of the above methods was depicted in **Scheme 1**.



Scheme 1

The benzodifurans were characterized by UV, IR, NMR and Mass spectral data (**Table 1**).

The UV spectra of all the compounds have displayed two absorption bands in the regions λ_{max} 322-327 and 355-359 nm as compared with unsubstituted benzofuran, which showed three absorption bands at λ_{max} 245, 275 and 282 nm. It is evident that all the bands in these benzodifurans (**3a-e**, **4a-g** and **5a-g**) are observed at longer wavelength region. This bathochromic shift is due to the presence of a second furan ring and two aroyl groups, which may facilitate the extended conjugation.

In the IR spectra of **3a-e**, **4a-g** and **5a-g** showed three bands were observed at 1600-1680 (C=O str), 1550-1590 (C=C str) and 1230-1260 cm^{-1}.

In the NMR spectra of the compounds, the ring closure and the linear nature of the benzodifurans were confirmed by the following observations.

(i) The protons at C4 and C8 positions were observed as singlets at δ 7.5-8.3

(ii) The four protons adjacent to aroyl group i.e., $C_{2',6',2'',6''}$ were observed as doublet at δ 7.8-8.3

Table I: Spectral Data of linear bisaroylbenzodifurans

BDF	U.V λ_{max} (nm)	I. R. (cm^{-1})	^{1}HNMR δ (ppm)	Mass m/z (% of abundance)	C, H, N, O Analysis Calc. (%)		Found (%)	
					C	H	C	H
3a (X= H) $C_{22}H_{18}O_4$	260, 322, 358	1640, 1560, 1250	7.9-8.1(d,4H,$C_{2',6',2'',6''}$); 7.95(s,1H,C_1); 7.4-7.6(m,7H,$C_{3',4',5',3'',4'',5''}$ & C_8) and 2.7(s, 6H, CH_3)	394(6); 365(23); 310(12); 158(22); 130(30);102(14); 105(56); 77(74)	79.18;	4.56	79.12;	4.90
3b (X= Cl) $C_{26}H_{16}Cl_2O_4$	258, 344	1680, 1590, 1250	8.1(d,4H,$C_{2',6',2'',6''}$);7.95(s,1H,C_1);7.6(s,1H C_1); 7.45(d,4H,$C_{3',5',3'',5''}$) and 2.7(s,6H,CH_3)	--	67.39,	3.46	67.36;	3.48
3c (X= Ph) $C_{38}H_{26}O_4$	262, 346	1630, 1580, 1260	8.15(d,4H,$C_{2',6',2'',6''}$),7.95(s,1H C_1);7.5(s,1H C_1); 7.45-7.55(m,10H);7.40(d,4H,$C_{3',5',3'',5''}$) and 2.75(s,6H,CH_3)	--	83.52;	4.76	83.54;	4.78
3d (X=2-OMe) $C_{32}H_{22}O_6$	265, 346	1645, 1585, 1260	8.2(d,4H,$C_{2',6',2'',6''}$),8.1(s,1H,C_1); 7.7-7.95(m,9H,$C_{4',5',7',8',4'',5'',7'',8''}$&$C_8$); 3.97(s,6H,$OCH_3$);2.8(s,6H,$CH_3$)	--	77.97;	4.73	77.94;	4.70
3e(X= NO_2) $C_{24}H_{16}N_2O_8$	258, 342	1620, 1570, 1250	8.35(d,4H,$C_{2',6',2'',6''}$); 8.3(s,1H,C_4);8.1(d,4H,$C_{3',5',3'',5''}$); 8.15(s,1H C_8) and 2.8(s,6H CH_3)	--	64.46;	3.31	64.42;	3.34
4a(X= H) $C_{28}H_{22}O_4$	258, 324, 360	1636, 1599, 1252	7.95-8.0(d,4H,$C_{2',6',2'',6''}$); 7.9(s,1H C_1); 7.4-7.6(m,7H,$C_{3',4',5',3'',4'',5''}$& C_8); 3.2(q,4H,CH_2) and 1.5(t,6H, CH_3)	422(4),366(25),338(12), 310(20),158(30),130(15), 105(75), 102(8), 77(55)	79.60;	5.25	79.58;	5.24
4b(X= Cl) $C_{28}H_{20}Cl_2O_4$	256, 340	1638, 1589, 1281	8.15-8.0(d,4H,$C_{2',6',2'',6''}$);7.9(s,1H,C_1); 7.5-7.15(m,5H,$C_{3',5',3'',5''}$&C_8); 3.22(q,4H,CH_2) and 1.55(t,6H, CH_3)	--	68.44;	4.10	68.40;	4.08
4c (X= Ph) $C_{40}H_{30}O_4$	260, 342	1642, 1604, 1280	8.05-8.0(d,4H,$C_{2',6',2'',6''}$); 7.9(s,1H,C_1); 7.55(s,1H,C_8); 7.4-7.6(m,10H);7.36(d,4H,$C_{3',5',3'',5''}$); 3.15(q,4H,CH_2) and 1.55(t,6H, CH_3)	--	83.60;	5.26	83.56;	5.25

4d (X=2-OMe) $C_{38}H_{30}O_6$	259, 340	1622, 1580, 1319, 1274	8.15-8.1(d,4H,$C_{1',3',1'',3''}$);8.05(s,1H,C_1); 7.6-7.9(m,9H,$C_{4',5',7,8,4'',5'',7'',8''}$,$C_8$);4.0(s,6H,$OCH_3$); 3.10(q,4H,$CH_2$) and 1.5(t,6H,$CH_3$)	—	78.33; 5.19	78.30; 5.15
4e(X=NO_2) $C_{38}H_{20}N_2O_8$	255, 345	1647, 1601, 1250	8.3-8.25(d,4H,$C_{2',6',2'',6''}$);8.05(s,1H,C_4); 8.0-7.95(d,4H,$C_{3',5',3'',5''}$);7.75(s,1H,C_1); 3.2(q,4H,CH_2) and 1.5(t,6H,CH_3)	—	65.62; 3.93	65.60; 3.91
4f(X=Me) $C_{30}H_{26}O_4$	256, 347	1633, 1604, 1252	7.95-7.9(d,4H,$C_{2',6',2'',6''}$);7.9(s,1H,C_4); 7.4-7.0(m,5H,$C_{3',5',3'',5''}$&C_8);3.2(q,4H,CH_2); 2.75(s,6H,CH_3) and 1.5(t,6H,CH_3)	—	79.98; 5.82	79.95; 5.80
4g(X=OMe) $C_{30}H_{26}O_6$	250, 340	1628, 1596, 1309, 1257	7.95-8.0(d,4H,$C_{2',6',2'',5''}$);7.8(s,1H,C_4); 7.45-7.4(m,5H,$C_{3',5',3'',5''}$&C_8);3.99(s,6H,OCH_3); 3.1(q,4H,CH_2) and 1.4(t,6H,CH_3)	—	74.67; 5.43	74.64; 5.40
5a(X=H) $C_{36}H_{22}O_4$	256, 325, 345	1652, 1598, 1236	8.15-8.10(d,4H,$C_{2',6',2'',5''}$);8.05(s,1H,C_4); 7.95-7.7(m,7H,$C_{3',4',5',3'',4'',5''}$&C_1);7.6-7.5(m,10H)	518(5),366(23),338(34), 310(12),158(45),130(35), 105(75),102(12),77(55)	83.38; 4.28	83.36; 4.25
5b(X=Cl) $C_{36}H_{20}Cl_2O_4$	258, 347	1646, 1587, 1235	8.15-8.10(d,4H,$C_{2',6',2'',6''}$);8.09(s,1H,C_4); 7.6-7.55(m,5H,$C_{3',5',3'',5''}$&C_8);7.65-7.6(m,10H)	—	73.60; 3.43	73.56; 3.40
5c(X=Ph) $C_{48}H_{30}O_4$	254, 348	1647, 1602, 1230	8.2-8.15(d,4H,$C_{2',6',2'',6''}$);8.10(s,1H,C_4); 7.95-7.75(m,5H,$C_{3',5',3'',5''}$&C_1);7.65-7.6(m,10H); 7.5-7.35(m,10H)	—	85.95; 4.51	85.94; 4.51
5d (X=2-OMe) $C_{46}H_{30}O_6$	255, 344	1621, 1554, 1272	8.05-8.0(d,4H,$C_{1',3',1'',3''}$);7.98(s,1H,C_1); 7.7-7.55(m,9H,$C_{4',5',7,8,4'',5'',7'',8''}$&$C_3$);7.55-7.45(m,10H); 4.1(s,6H,OCH_3)	—	81.40; 4.46	81.35; 4.42
5e(X=NO_2) $C_{36}H_{20}N_2O_8$	252, 341	1635, 1607, 1260	8.25-8.20(d,4H,$C_{2',6',2'',6''}$);8.15(s,1H,C_4);7.95(s,1H,C_8); 7.7-7.5(d,4H,$C_{3',5',3'',5''}$);7.65-7.6(m,10H)	—	71.05; 3.31	71.02; 3.30
5f(X=Me) $C_{38}H_{26}O_4$	253, 340	1640, 1606, 1235	8.2-8.15(d,4H,$C_{2',6',2'',6''}$);8.1(s,1H,C_1); 7.8-7.65(m,5H,$C_{3',5',3'',5''}$&C_8); 7.55-7.4(m,10H);2.65(s,6H,CH_3)	—	83.50; 4.79	83.45; 4.75
5g(X=OMe) $C_{38}H_{28}O_6$	256, 342	1645, 1601, 1260	8.1-8.05(d,4H,$C_{2',6',2'',6''}$);8.0(s,1H,C_1); 7.7-7.6(m,5H,$C_{3',5',3'',5''}$&C_8); 7.4-7.3(m,10H);4.2(s,6H,OCH_3)	—	78.88; 4.53	78.85; 4.52

Table 2: Biological activity of linear bisaroylbenzodifurans

BDF	M.P. (°C)	PTC Rn time (Hrs.)	Yield (%)	MW Time (min)	Yield (%)	Conc µg/ml	Anti - Bacterial activity								Anti-implantation at 10 mg/kg
							Bac1	Bac2	Bac3	Bac4	Bac5	Bac6	Bac7	Bac8	Efficacy (%)
3a	185-7	6.0	92.7	1.5	96.4	600	1.96	3.84	1.96	1.13	0.94	NA	0.31	1.96	
						900	3.84	6.35	7.85	1.53	1.13	0.12	1.2	1.96	
3b	126-8	6.5	85.0	2.0	93.5	600	3.84	0.70	0.7	NA	1.13	NA	NA	0.12	
						900	6.35	3.84	1.96	0.7	1.32	0.7	0.12	0.28	
3c	158-9	6.0	87.3	2.0	95.0	600	1.96	1.96	1.96	0.7	5.02	NA	1.96	1.96	
						900	3.84	6.35	3.84	3.84	6.35	0.7	3.84	3.84	
3d	232-5	6.0	90.4	2.5	97.9	600	3.84	NA	0.7	6.35	6.35	3.84	1.96	0.70	
						900	7.85	0.7	3.84	7.85	7.85	5.02	5.02	2.82	
3e	136-8	7.0	84.0	3.0	89.6	600	0.31	NA	1.25	5.02	5.02	5.02	6.35	3.84	
						900	1.96	0.7	5.02	6.35	6.35	6.35	7.85	6.35	
4a	157-8	6.0	94.0	2.5	95.8	600	1.96	1.96	0.7	1.96	1.96	5.02	5.02	1.96	Inactive
						900	3.84	5.02	1.25	5.02	6.35	6.35	6.35	3.84	
4b	202-3	6.5	92.4	3.0	93.0	600	3.84	NA	1.96	0.7	3.84	6.35	6.35	1.96	—
						900	7.85	NA	5.02	1.25	5.02	9.49	7.85	3.84	
4c	211-3	7.0	90.8	3.0	94.7	600	1.96	2.82	2.82	1.25	2.82	2.82	1.96	5.02	67
						900	5.02	3.84	5.02	1.96	3.84	5.02	3.84	6.35	
4d	177-9	7.5	94.5	3.0	96.5	600	5.02	NA	NA	1.96	2.82	3.84	1.96	1.96	Inactive
						900	6.35	0.7	1.25	2.82	5.02	7.85	5.02	3.84	
4e	177-9	8.0	87.0	2.5	89.0	600	NA	NA	NA	NA	0.78	1.96	1.25	1.96	—
						900	NA	NA	NA	NA	1.13	2.82	2.82	2.82	
4f	156-7	6.0	87.5	2.0	90.1	600	1.96	1.96	0.7	1.96	1.96	5.02	5.02	1.96	Inactive
						900	3.84	5.02	1.25	5.02	6.35	6.35	6.35	3.84	
4g	177-9	6.0	91.2	1.5	93.9	600	1.96	1.96	0.7	0.7	NA	1.25	1.25	3.84	Inactive
						900	2.82	2.82	1.96	3.84	0.7	1.96	1.96	5.02	
5a	208-9	6.0	91.4	3.0	93.3	600	--	--	—	—	—	--	—	--	Inactive
						900	—	--	—	--	—	--	--	--	
5b	184-6	6.5	90.6	3.0	92.9	600	1.96	5.02	3.84	5.02	1.96	1.96	2.82	5.02	—
						900	2.82	6.35	5.02	6.85	3.84	3.84	5.02	6.35	

5c	210-2	6.0	93.7	3.0	94.1	600	1.96	1.96	3.84	1.96	0.7	NA	1.25	1.25		Inactive
						900	3.84	2.82	5.02	2.82	1.95	0.7	2.82	1.96		
5d	148-9	7.0	95.6	3.0	96.2	600	5.02	NA	NA	NA	NA	NA	1.25	1.96		Inactive
						900	6.35	NA	NA	NA	NA	NA	2.82	5.02		
5e	77-9	7.5	87.5	3.0	88.3	600	0.70	NA	NA	0.31	1.96	1.96	3.84	1.96		---
						900	2.82	0.31	1.96	1.25	5.02	5.02	5.02	3.84		
5f	180-2	6.0	87.9	2.0	89.0	600	3.84	5.02	1.96	1.96	1.25	1.25	1.25	0.7		---
						900	5.02	6.35	3.84	5.02	2.82	2.82	3.84	1.96		
5g	126-8	6.0	90.0	3.0	91.0	600	0.70	1.96	2.82	5.02	3.84	3.84	5.02	1.96		Inactive
						900	2.82	3.84	3.84	6.35	6.35	6.35	6.35	3.84		
Std	---	---	---	---	---	600	6.77	4.70	6.77	NA	4.2	3.0	5.52	5.52		---
						900	10.1	7.05	10.1	NA	6.3	4.5	8.28	8.28		

BDF Linear bis aroyl benzodifuran PTC Phase Transfer catalysis method MW Microwave irradiation method

Bac1: Escherichia Coli Bac2: Proteus Vulgaris Bac3: Klebsiella Pneumoniae

Bac4: Pseudomonas Aerurinosa Bac5: Staphylococcus Citricus Bac6: Staphylococcus Aureus

Bac7: Bacillus Subtilis Bac8: Streptococcus Albus Std: Streptomycin

Rn Time: Reaction Time NA No activity

Ar =naphthalene (in case of **3d**, **4d** and **5d**)

(iii) The protons of $C_{3',5',3'',5''}$ were observed as doublet at δ 7.3-8.1. Whereas in **3a**, **4a** and **5a** a multiplet was observed at δ 7.4-7.7 for protons of $C_{3',4',5',3'',4''5''}$

Experimental

Melting points were determined in open capillaries and were uncorrected. The UV spectra were recorded on Shimadzu UV 160A UV-Vis-NIR spectrophotometer, IR spectra on Shimadzu FTIR model 8010 spectrophotometer and the 1H NMR spectra in $CDCl_3$ on Varion C17-20-ZM-390-200 MHz NMR spectrophotometer using TMS as an internal standard. Mass spectra were recorded on VG 7070H ion analyzer. The C, H and O analysis of the compounds was done on a Carlo Erba Model EA 1108 CHNS-O elemental analyzer.

General Experimental Procedure for Phase transfer catalysis method:

To a magnetically stirred solution of diacyl /aroyl resorcinols (1 **i-iii**; 0.01 mole) in 30 ml ethylenedichloride, 30 ml of aq. 20% K_2CO_3 solution and 100mg tetrabutyl ammonium hydrogen sulphate were added. The reaction mixture was heated to 50^0 and the various *p*-substituted phenacyl bromides (**2a-g**; 0.02 mole) were added drop wise over a period of 30 minutes at $55\text{-}60^0$ and the temperature was maintained for 6-8 hours. The organic layer was separated, washed with 5% NaOH solution and then with water. The resulting organic layer was dried over anhydrous sodium sulphate. The excess solvent was removed under reduced pressure and the crude product was crystallized from methanol.

General experimental procedure for microwave irradiation:

Diacyl/ aroyl resorcinols (**1i-iii**; 0.01 mole) and various substituted α-bromoketones (**2a-g**; 0.02 mole) were doped with baked K_2CO_3 and were irradiated in microwave oven for 1-3 minutes. The reaction was monitored by TLC. After irradiation, the crude was poured into water to remove the inorganic matter. The resultant product was crystallized from methanol.

Anti-Bacterial Activity

The bisaroylbenzodifurans (**3a-e**, **4a-g** and **5a-g**) were tested on four-gram positive bacteria (*Staphylococcus citricus*, *Staphylococcus aureus*, *Bacillus subtilis*, *Streptococcus albus*) and also on four gram negative bacteria (*Escherichia coli*, *Proteus vulgaris*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*) at concentrations 600 and 900 μg/ ml, by adopting Vincent and Vincent filter paper disc method (16). The results were depicted in **Table 2**.

2,6-diaroyl/naphthoyl-3,5-dimethyl-benzo[1,2-b;5,4-b']difurans (**3a-e**) have not shown marked activity against the gram negative bacteria-*Escherichia coli*, *Proteus vulgaris* and *Klebsiella pneumoniae* at both 600 and 900 μg/ ml . Interestingly streptomycin is not active against *Pseudomonus aeruginosa* bacteria, whereas all the benzodifurans **3a-e**, **4a-g** and **5a-g** have shown activity against *Pseudomonus aeruginosa* bacteria. Among all the bis aroylbenzodifurans (**3a-e**) with methyl substitution at 3 and 5 positions, 2,6-di(6-methoxy 2-naphthoyl)-3,5-dimethyl-benzo[1,2-b; 5,4-b']difuran (**3d**) has shown the highest percentage of activity against *Pseudomonus aeruginosa* bacteria

All the benzodifurans **3a-e** have been observed to be very active against gram positive - bacteria *Staphylococcus citricus*, *Staphylococcus aureus* and *Bacillus subtilis*. Among these bisaroylbenzodifuans, **3c**, **3d** and **3e** have shown high percentage of activity at both concentration levels against *Staphylococcus citricus* bacteria. The compounds **3d** and **3e** have shown very good activity at both concentration levels against *Staphylococcus aureus*. Among all the bisaroylbenzodifurans (**3a-e**) with methyl substitution at 3 and 5 positions, 2,6-di(6-methoxy-2-naphthoyl)-3,5-dimethyl-benzo[1,2-b; 5,4-b']difuran (**3d**) has shown the highest activity against

Staphylococcus citricus bacteria with reference to all the gram positive bacteria. In the 2,6-diaroyl/naphthoyl-3,5-diethyl-benzo[1,2-b;5,4-b']difurans (**4a-g**), only two compounds **4b** and **4d** have shown marginal activity against the gram negative bacteria at both concentration levels. The remaining compounds were inactive. The bisaroyl benzodifurans, **4a**, **4b**, **4d** and **4f** have shown very good activity against *Staphylococcus aureus* bacteria at both concentration levels. Among these, **4b** is found to be the highest active compound in the both concentration levels. The bisaroylbenzodifurans (**5a-g**) were found inactive against gram negative bacteria. Only one compound, 2,6-di(*p*-methoxy benzoyl)-3,5-diphenyl-benzo[1,2-b;5,4-b']difuran (**5g**) has shown very good activity against *Bacillus subtilis* at both concentrations and the remaining were found inactive against all the gram positive bacteria.

It is evident from the above observations that, most of the aroyl benzodifurans were active against gram-positive bacteria rather than gram-negative bacteria. Among all the active bisaroylbenzodifurans, 2,6-di(6-methoxy-2-naphthoyl)-3,5-dimethyl-benzo[1,2-b;5,4-b'] difuran (**3d**) has shown very good activity against all the gram positive bacteria. It is generally observed that the percentage of activity is decreased when ethyl/ phenyl group replaces the methyl group at 3,5-bisaroylbenzodifuran positions.

Anti-implantation activity

Linear bisaroylbenzodifurans (**3a-e**) were reported for anti-implantation activity. By following the same reported procedure[9], some of the selected compounds in **4a-g** & **5a-g** series were screened for anti-implantation activity. Only one compound (**4c**) has shown 67% activity. Remaining compounds were found inactive at 10 mg/kg/rat/day on albino rats. The results were shown in **Table 2**.

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