Synthesis of Novel Antibacterial Agents: 1-(2', 4'-Dihydroxy-5'-chlorophenyl)-3- arylpropane-1, 3-diones

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Abstract: 1-(2', 4'-Dihydroxy-5'-chlorophenyl)-3-arylpropane-1, 3-diones (**3a-h**) have been synthesized by a simple and convenient method employing Baker-Venkatraman transformation on 2-aryloxy-4-hydroxy-5-chloroacetophenones (**2a-h**) with NaOH in dimethylsulphoxide regardless of pyridine. The structures of the synthesized compounds have been assigned on the basis of elemental and spectral analyses (IR, ¹HNMR, ¹³C NMR, Mass). The synthesized compounds were evaluated for the antibacterial efficacy against gram negative and gram positive bacteria.

Keywords: β -Diketones, Dibenzoylmethanes, Esterification, Baker-Venkatraman transformation, Antibacterial activity.

Introduction

β -Diketones are key intermediates for the synthesis of core heterocycles such as pyrazole¹, isoxazole², triazole³, flavone⁴, benzodiazepine⁵ and pyrimidine⁶. They have been shown to have varying degree of pharmacological activities like antibacterial⁷, antiviral⁸, insecticidal⁹, antioxidant¹⁰ and potential prophylactic antitumor activity¹¹. It has also been used as anti-sunscreen agent¹². Dibenzoylmethane (DBM), a β -diketone analogue of curcumin, has antimutagenic activity and demonstrated that DBM inhibits 7, 12-dimethylbenz[α]anthracene (DMBA)-induced breast tumorigenesis in mice¹³. Singletary et al. have shown that DBM has potent chemopreventive activity against DMBA-induced carcinogenesis in rat^{14,15}. Also β -ketoenols are important pharmacophores of HIV-1 integrase (IN) inhibitors¹⁶.

In light of these results and as the chemist would not stop at β -diketones having such varying pharmacological activities and in continuation of our earlier research work on β -diketones oriented our attention to synthesize a series of new 1-(2', 4'-dihydroxy-5'-chlorophenyl)-3-aryl-propane-1, 3-diones (**3a-h**). Herein, we aimed to report the synthesis and antibacterial activity of **3a-h** which are obtained via simple and convenient method using Baker-Venkatraman rearrangement with NaOH in DMSO¹⁷, despite the use of pyridine having unpleasant odour and not so easy to remove from the reaction mixture. The 2-aryloxy-4-hydroxy-5-chloroacetophenones (**2a-h**), the precursor of **3a-h** was previously obtained by conventional method.

Experimental

2, 4-Dihydroxy-5-chloroacetophenone (**1**) was prepared by Nenki reaction from 4-chlororesorcinol and glacial acetic acid¹⁸. 4-chlororesorcinol, POCl₃, DMSO, different aromatic carboxylic acids and all other chemical used where of synthetic grade obtained from the local dealer.

Measurements

Melting points were determined in open glass capillaries and were uncorrected. Elemental analyses were determined using the Perkin Elmer 2400 CHN analyzer. FT-IR spectra were recorded using (KBr) disc on Perkin-Elmer spectrum Rx-I spectrometer. ¹H NMR and ¹³C NMR were recorded on Bruker AC-300 F (300 MHz) NMR spectrometer by using DMSO-d₆ and CDCl₃ as solvent and tetramethylsilane as an internal standard. Mass spectra were recorded on 70-S Mass spectrometer using m-nitro benzyl alcohol (NBA) matrix.

Preparation of 2-aryloxy-4-hydroxy-5-chloroacetophenones (**2a-h**)

2, 4-Dihydroxy-5-chloroacetophenone **1** (0.01 mol) and aromatic carboxylic acid (0.01 mol) were dissolved in 5 mL of redistilled pyridine and cooled, to that POCl₃ 1 mL was added drop wise with constant stirring maintaining the temperature below 20 °C. The reaction mixture was kept overnight at room temperature and poured with stirring on ice cold dil HCl (1 mol in 50 mL). A white granulated solid compound **2a-h** separated out which was washed with cold water, dil. NaHCO₃ solution and again with cold water. The product was filtered off, dried and recrystallized from alcohol. It gave positive test for ester. It was obtained in 65-76% yield. The physical and analytical data of the compounds **2a-h** are given in Table 1. The spectral data for various **2a-h** are described below.

Table 1. The physical and analytical data of compounds (**2a-h**).

Compd	Molecular Formula	Mol. Wt.	Yield, %	M. P. °C	% Analysis			
					%C		%H	
					Cald	Found	Cald	Found
2a	C ₁₅ H ₁₁ ClO ₄	290.5	70	113	61.98	62.06	3.81	3.90
2b	C ₁₅ H ₁₀ Cl ₂ O ₄	324	64	115	55.41	55.56	3.10	3.14
2c	C ₁₅ H ₁₀ Cl ₂ O ₄	324	69	153	55.41	55.46	3.10	3.16
2d	C ₁₅ H ₁₀ Cl ₂ O ₄	324	73	185	55.41	55.39	3.10	3.09
2e	C ₁₆ H ₁₃ ClO ₅	320.5	67	119	59.92	60.00	4.09	4.12
2f	C ₁₆ H ₁₃ ClO ₅	320.5	63	78	59.92	59.98	4.09	4.16
2g	C ₁₆ H ₁₃ ClO ₄	304.5	65	121	63.06	63.14	4.30	4.42
2h	C ₁₆ H ₁₃ ClO ₄	304.5	71	147	63.06	63.01	4.30	4.48

2a: FT-IR (KBr): 3419 (OH), 1759 (ester C=O), 1697 (C=O), 1603 (aromatic C=C), 1144 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.59 (s, 3H, CH_3), 4.86 (s, 1H, OH), 8.09 (d, 2H, $J_{2-6}=7.9$ Hz, 2'-H, 6'-H), 6.73-7.93 (m, 5H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 198.7 (s, C-7, C=O), 154.7 (s, C-2, C-O), 165.8 (s, C-9, C=O), 130.6 (s, C-1'), 131.7 (s, C-2', C-6'), 128.2 (s, C-3', C-5'), 134.1 (s, C-4'), 29.2 (s, CH_3 of C-8), 120.9 (s, C-1), 110.5 (s, C-3), 164 (s, C-4), 120.1 (s, C-5), 131 (s, C-6); MS (EI, 70eV): m/z (%) 290 (M^+ , 100), 292 (32), 105 (57), 51 (19).

2b: FT-IR (KBr): 3421 (OH), 1760 (ester C=O), 1687 (C=O), 1602 (aromatic C=C), 1131 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.67 (s, 3H, CH_3), 4.85 (s, 1H, OH), 6.77-8.09 (m, 6H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 199.1 (s, C-7, C=O), 155.7 (s, C-2, C-O), 165.1 (s, C-9, C=O), 130.5 (s, C-1'), 134.7 (s, C-2'), 128.6 (s, C-3'), 135.1 (s, C-4'), 127 (s, C-5'), 131.1 (s, C-6'), 29.2 (s, CH_3 of C-8), 119 (s, C-1), 108.9 (s, C-3), 164.2 (s, C-4), 121.2 (s, C-5), 130.9 (s, C-6); MS (EI, 70eV): m/z (%) 324 (M^+ , 100), 326 (63), 105 (51), 51 (16).

2c: FT-IR (KBr): 3425 (OH), 1763 (ester C=O), 1680 (C=O), 1599 (aromatic C=C), 1140 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.57 (s, 3H, CH_3), 4.91 (s, 1H, OH), 6.73-8.11 (m, 6H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 198.2 (s, C-7, C=O), 154.9 (s, C-2, C-O), 166.3 (s, C-9, C=O), 130.9 (s, C-1'), 134.2 (s, C-2'), 130.6 (s, C-3'), 135.2 (s, C-4'), 128 (s, C-5'), 130.9 (s, C-6'), 28.8 (s, CH_3 of C-8), 118.3 (s, C-1), 109.2 (s, C-3), 165.1 (s, C-4), 120.7 (s, C-5), 131.2 (s, C-6); MS (EI, 70eV): m/z (%) 324 (M^+ , 100), 326 (56), 105 (49), 51 (13).

2d: FT-IR (KBr): 3429 (OH), 1762 (ester C=O), 1689 (C=O), 1602 (aromatic C=C), 1139 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.61 (s, 3H, CH_3), 4.81 (s, 1H, OH), 8.06 (d, 2H, $J_{2-6}=8.4$ Hz, 2'-H, 6'-H), 7.47 (d, 2H, $J_{3-5}=8.4$ Hz, 3'-H, 5'-H), 6.69-7.74 (m, 3H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 199.1 (s, C-7, C=O), 154.7 (s, C-2, C-O), 165.4 (s, C-9, C=O), 129.4 (s, C-1'), 130.8 (s, C-2', C-6'), 128.7 (s, C-3', C-5'), 138.3 (s, C-4'), 29.8 (s, CH_3 of C-8), 120.1 (s, C-1), 109.5 (s, C-3), 164.1 (s, C-4), 119.7 (s, C-5), 130.2 (s, C-6); MS (EI, 70eV): m/z (%) 324 (M^+ , 100), 326 (53), 105 (42), 51 (18).

2e: FT-IR (KBr): 3422 (OH), 1760 (ester C=O), 1681 (C=O), 1600 (aromatic C=C), 1143 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.53 (s, 3H, CH_3), 4.99 (s, 1H, OH), 7.02-7.79 (m, 6H, Ar-H), 3.73 (s, 3H, 3'- OCH_3); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 199.0 (s, C-7, C=O), 155.9 (s, C-2, C-O), 166.8 (s, C-9, C=O), 131.1 (s, C-1'), 114.2 (s, C-2'), 160.6 (s, C-3'), 119.2 (s, C-4'), 129.7 (s, C-5'), 122.9 (s, C-6'), 29.4 (s, CH_3 of C-8), 119.3 (s, C-1), 109.8 (s, C-3), 164.3 (s, C-4), 119.9 (s, C-5), 130.2 (s, C-6), 56.2 (s, OCH_3 of C-7'); MS (EI, 70eV): m/z (%) 320 (M^+ , 100), 322 (36), 105 (47), 51 (11).

2f: FT-IR (KBr): 3433 (OH), 1766 (ester C=O), 1685 (C=O), 1603 (aromatic C=C), 1144 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.59 (s, 3H, CH_3), 4.89 (s, 1H, OH), 8.04 (d, 2H, $J_{2-4}=8.1$ Hz, 2'-H, 4'-H), 7.01 (d, 2H, $J_{3-5}=8.1$ Hz, 3'-H, 5'-H), 6.68-7.76 (m, 3H, Ar-H), 3.69 (s, 3H, 4'- OCH_3); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 199.7 (s, C-7, C=O), 155.7 (s, C-2, C-O), 164.4 (s, C-9, C=O), 122.4 (s, C-1'), 131.8 (s, C-2', C-6'), 114.7 (s, C-3', C-5'), 165.3 (s, C-4'), 29.1 (s, CH_3 of C-8), 120.4 (s, C-1), 108.7 (s, C-3), 164.1 (s, C-4), 121.1 (s, C-5), 130.9 (s, C-6), 56.1 (s, OCH_3 of C-7'); MS (EI, 70eV): m/z (%) 320 (M^+ , 100), 322 (32), 105 (46), 51 (14).

2g: FT-IR (KBr): 3430 (OH), 1767 (ester C=O), 1689 (C=O), 1603 (aromatic C=C), 1146 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.58 (s, 3H, CH_3), 4.83 (s, 1H, OH), 6.79-7.94 (m, 6H, Ar-H), 2.46 (s, 3H, 3'- CH_3); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 199.6 (s, C-7, C=O), 154.9 (s, C-2, C-O), 166.2 (s, C-9, C=O), 130.1 (s, C-1'), 130.2 (s, C-2'), 138.6 (s, C-3'), 134.2 (s, C-4'), 128.7 (s, C-5'), 127.9 (s, C-6'), 29.1 (s, CH_3 of C-8), 120.3 (s, C-1), 109.6 (s, C-3), 164.7 (s, C-4), 122.9 (s, C-5), 130.8 (s, C-6), 24.8 (s, CH_3 of C-7'); MS (EI, 70eV): m/z (%) 304 (M^+ , 100), 306 (31), 105 (60), 51 (21), 15 (11).

2h: FT-IR (KBr): 3440 (OH), 1767 (ester C=O), 1680 (C=O), 1601 (aromatic C=C), 1141 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 2.52 (s, 3H, CH_3), 4.80 (s, 1H, OH), 8.01 (d, 2H, $J_{2,4}=8.6$ Hz, 2'-H, 4'-H), 7.19 (d, 2H, $J_{3,5}=8.6$ Hz, 3'-H, 5'-H), 6.79-7.73 (m, 3H, Ar-H), 2.43 (s, 3H, 4'- CH_3); ^{13}C NMR (DMSO- d_6 , 300 MHz) δ : 199.1 (s, C-7, C=O), 155.2 (s, C-2, C-O), 166.4 (s, C-9, C=O), 122.3 (s, C-1'), 130.4 (s, C-2', C-6'), 129.7 (s, C-3', C-5'), 143.3 (s, C-4'), 29.5 (s, CH_3 of C-8), 120.2 (s, C-1), 108.8 (s, C-3), 164.4 (s, C-4), 113.1 (s, C-5), 131.9 (s, C-6), 24.1 (s, CH_3 of C-7'); MS (EI, 70eV): m/z (%) 304 (M^+ , 100), 306 (33), 105 (51), 51 (18), 15 (14).

1-(2', 4'-Dihydroxy-5'-chlorophenyl)-3-phenyl-propane-1, 3-diones (3a-h)

The product **2a-h** (0.005 mol) was dissolved in 4 mL of DMSO. To that solution, powdered NaOH (1 g) was added with vigorous stirring for about 5 min. The stirring was continued for about 5 min further. The reaction mixture was then cooled and poured on cold water. The pale yellow solid product obtained was washed with water and filtered off. It was crystallized from alcohol. The yield was 64-72%. The physical and analytical data of the compounds **3a-h** are given in Table 2. The spectral data for different **3a-h** are described below.

Table 2. The physical and analytical data of Compounds **3a-h**

Compd	Molecular Formula	Mol. Wt.	Yield %	M. P. $^{\circ}\text{C}$	% Analysis			
					%C		%H	
					Cald	Found	Cald	Found
3a	$\text{C}_{15}\text{H}_{11}\text{ClO}_4$	290.5	70	134	61.98	62.01	3.81	3.98
3b	$\text{C}_{15}\text{H}_{10}\text{Cl}_2\text{O}_4$	324	63	120	55.41	55.52	3.10	3.16
3c	$\text{C}_{15}\text{H}_{10}\text{Cl}_2\text{O}_4$	324	69	145	55.41	55.56	3.10	3.19
3d	$\text{C}_{15}\text{H}_{10}\text{Cl}_2\text{O}_4$	324	73	210	55.41	55.49	3.10	3.13
3e	$\text{C}_{16}\text{H}_{13}\text{ClO}_5$	320.5	68	146	59.92	60.06	4.09	4.20
3f	$\text{C}_{16}\text{H}_{13}\text{ClO}_5$	320.5	71	132	59.92	59.96	4.09	4.25
3g	$\text{C}_{16}\text{H}_{13}\text{ClO}_4$	304.5	67	161	63.06	63.16	4.30	4.34
3h	$\text{C}_{16}\text{H}_{13}\text{ClO}_4$	304.5	71	140	63.06	63.09	4.30	4.43

3a: FT-IR (KBr): 3438 (OH), 1743 (C=O), 1599 (aromatic C=C), 1142 (C-O); ^1H NMR (DMSO- d_6 , 300MHz,) δ : 15.72 (s, 1H, enolic OH), 12.02 (s, 1H, 2'-OH), 4.76 (s, 1H, 4'-OH), 8.17 (s, 1H, -CH=), 7.10 (d, 2H, $J_{2'',6''}=8.4$ Hz, 2''-H, 6''-H), 6.89-8.02 (m, 5H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 192.1 (s, C-1, C=O), 178.4 (s, C-3), 93.0 (s, C-2, -CH=), 112.7 (s, C-1'), 162.2 (s, C-2'), 110.6 (s, C-3'), 160.7 (s, C-4'), 116.8 (s, C-5'), 133.5 (s, C-6'), 130.1 (s, C-1''), 126.5 (s, C-2'', C-6''), 128.3 (s, C-3'', C-5''), 129.6 (s, C-4''); MS (EI, 70eV): m/z (%) 290 (M^+ , 100), 292 (31), 224 (29), 105 (58), 51 (15).

3b: FT-IR (KBr): 3430 (OH), 1739 (C=O), 1601 (aromatic C=C), 1144 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 15.81 (s, 1H, enolic OH), 12.05 (s, 1H, 2'-OH), 4.80 (s, 1H, 4'-OH), 8.29 (s, 1H, -CH=), 6.57-7.41 (m, 6H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 190.5 (s, C-1, C=O), 182.1 (s, C-3), 93.2 (s, C-2, -CH=), 115.3 (s, C-1'), 163.4 (s, C-2'), 109.1 (s, C-3'), 161.2 (s, C-4'), 116.4 (s, C-5'), 133.1 (s, C-6'), 131.7 (s, C-1''), 131.2 (s, C-2''), 128.8 (s, C-3''), 129.6 (s, C-4''), 126.8 (s, C-5''), 130.7 (s, C-6''); MS (EI, 70eV): m/z (%) 324 (M^+ , 100), 326 (61), 224 (32), 105 (55), 51 (11).

3c: FT-IR (KBr): 3433 (OH), 1741 (C=O), 1600 (aromatic C=C), 1143 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 15.91 (s, 1H, enolic OH), 12.01 (s, 1H, 2'-OH), 4.89 (s, 1H, 4'-OH), 8.31 (s, 1H, -CH=), 6.59-7.32 (m, 6H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 190.1 (s, C-1, C=O), 185.2 (s, C-3), 93.4 (s, C-2, -CH=), 115.9 (s, C-1'), 163.2 (s, C-2'), 108.3 (s, C-3'), 160.2 (s, C-4'), 117.2 (s, C-5'), 132.7 (s, C-6'), 131.8 (s, C-1''), 126.2 (s, C-2''), 134.4 (s, C-3''),

128.4 (s, C-4"), 130.8 (s, C-5"), 124.4 (s, C-6"); MS (EI, 70eV): m/z (%) 324 (M^+ , 100), 326 (59), 224 (37), 105 (49), 51 (14).

3d: FT-IR (KBr): 3429 (OH), 1736 (C=O), 1604 (aromatic C=C), 1149 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 15.99 (s, 1H, enolic OH), 12.09 (s, 1H, 2'-OH), 4.76 (s, 1H, 4'-OH), 8.41 (s, 1H, -CH=), 7.36 (d, 2H, $J_{2''-4''}$ = 7.9 Hz, 2''-H, 4''-H), 7.32 (d, 2H, $J_{3''-5''}$ = 7.8 Hz, 3''-H, 5''-H), 6.67-7.42 (m, 3H, Ar-H); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 189.7 (s, C-1, C=O), 184.3 (s, C-3), 94.1 (s, C-2, -CH=), 116.4 (s, C-1'), 163.6 (s, C-2'), 107.5 (s, C-3'), 161.7 (s, C-4'), 117.5 (s, C-5'), 132.1 (s, C-6'), 128.4 (s, C-1''), 127.4 (s, C-2'', C-6''), 129.8 (s, C-3'', C-5''), 131.5 (s, C-4''); MS (EI, 70eV): m/z (%) 324 (M^+ , 100), 326 (57), 224 (32), 105 (51), 51 (14).

3e: FT-IR (KBr): 3428 (OH), 1745 (C=O), 1606 (aromatic C=C), 1145 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 16.01 (s, 1H, enolic OH), 12.05 (s, 1H, 2'-OH), 4.89 (s, 1H, 4'-OH), 8.49 (s, 1H, -CH=), 6.45-7.51 (m, 6H, Ar-H), 3.79 (s, 3H, 3''-OCH₃); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 190.1 (s, C-1, C=O), 182.9 (s, C-3), 93.5 (s, C-2, -CH=), 115.6 (s, C-1'), 163.7 (s, C-2'), 106.9 (s, C-3'), 163.2 (s, C-4'), 115.8 (s, C-5'), 132.7 (s, C-6'), 131.4 (s, C-1''), 110.2 (s, C-2''), 160.4 (s, C-3''), 113.4 (s, C-4''), 129.8 (s, C-5''), 118.4 (s, C-6''), 55.9 (s, OCH₃ of C-7''); MS (EI, 70eV): m/z (%) 320 (M^+ , 100), 322 (30), 224 (32), 105 (43), 51 (13).

3f: FT-IR (KBr): 3423 (OH), 1729 (C=O), 1600 (aromatic C=C), 1139 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 15.99 (s, 1H, enolic OH), 12.29 (s, 1H, 2'-OH), 4.68 (s, 1H, 4'-OH), 8.59 (s, 1H, -CH=), 7.20 (d, 2H, $J_{2''-4''}$ = 8.1 Hz, 2''-H, 4''-H), 7.19 (d, 2H, $J_{3''-5''}$ = 8.1 Hz, 3''-H, 5''-H), 6.49-7.41 (m, 3H, Ar-H), 3.65 (s, 3H, 4''-OCH₃); ^{13}C NMR (300MHz, DMSO- d_6) δ : 189.3 (s, C-1, C=O), 184.9 (s, C-3), 94 (s, C-2, -CH=), 116.3 (s, C-1'), 163.9 (s, C-2'), 106.5 (s, C-3'), 162.7 (s, C-4'), 115.4 (s, C-5'), 131.2 (s, C-6'), 122.4 (s, C-1''), 127.8 (s, C-2'', C-6''), 114.8 (s, C-3'', C-5''), 159.5 (s, C-4''), 56 (s, OCH₃ of C-7''); MS (EI, 70eV): m/z (%) 320 (M^+ , 100), 322 (32), 224 (21), 105 (66), 51 (20).

3g: FT-IR (KBr): 3439 (OH), 1744 (C=O), 1603 (aromatic C=C), 1148 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 16.03 (s, 1H, enolic OH), 12.01 (s, 1H, 2'-OH), 4.78 (s, 1H, 4'-OH), 8.59 (s, 1H, -CH=), 6.46-7.47 (m, 6H, Ar-H), 2.59 (s, 3H, 3''-CH₃); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 189.9 (s, C-1, C=O), 184.7 (s, C-3), 93.8 (s, C-2, -CH=), 115.9 (s, C-1'), 164.7 (s, C-2'), 104.1 (s, C-3'), 161.3 (s, C-4'), 116.2 (s, C-5'), 131.9 (s, C-6'), 130.4 (s, C-1''), 126.2 (s, C-2''), 138.4 (s, C-3''), 128.4 (s, C-4''), 128.8 (s, C-5''), 123.4 (s, C-6''), 24.8 (s, CH₃ of C-7''); MS (EI, 70eV): m/z (%) 304 (M^+ , 100), 306 (29), 224 (29), 105 (55), 51 (16).

3h: FT-IR (KBr): 3425 (OH), 1723 (C=O), 1602 (aromatic C=C), 1140 (C-O); ^1H NMR (DMSO- d_6 , 300MHz) δ : 15.97 (s, 1H, enolic OH), 12.12 (s, 1H, 2'-OH), 4.78 (s, 1H, 4'-OH), 8.43 (s, 1H, -CH=), 7.19 (d, 2H, $J_{2''-4''}$ = 8.6 Hz, 2''-H, 4''-H), 7.11 (d, 2H, $J_{3''-5''}$ = 8.6 Hz, 3''-H, 5''-H), 6.42-7.39 (m, 3H, Ar-H), 2.52 (s, 3H, 4''-CH₃); ^{13}C NMR (DMSO- d_6 , 300MHz) δ : 189.6 (s, C-1, C=O), 184.5 (s, C-3), 94.2 (s, C-2, -CH=), 116.3 (s, C-1'), 164.3 (s, C-2'), 105.6 (s, C-3'), 160.7 (s, C-4'), 114.6 (s, C-5'), 131.6 (s, C-6'), 127.4 (s, C-1''), 126.8 (s, C-2'', C-6''), 129.2 (s, C-3'', C-5''), 137.5 (s, C-4''), 24.4 (s, CH₃ of C-7''); MS (EI, 70eV): m/z (%) 304 (M^+ , 100), 306 (25), 224 (24), 105 (59), 51 (19).

Results and Discussion

The 2-aryloxy-4-hydroxy-5-chloroacetophenones **2a-h** were prepared by the esterification of 2, 4-dihydroxy-5-chloroacetophenone **1** with aromatic carboxylic acids in the presence of POCl₃ (Scheme 1). 1-(2', 4'-Dihydroxy-5'-chlorophenyl)-3-aryl-propane-1, 3-diones **3a-h** were prepared by Baker-Venkatraman Transformation (intramolecular Claisen condensation) of **2a-h** with NaOH in DMSO. The ^1H NMR spectrum of **3a** exhibited a singlet at δ 15.72 ppm due to enolic proton (since enol form in β -diketone is more stable), a singlet at δ 12.02 ppm due to

phenolic proton adjacent to the carbonyl group and a singlet at δ 4.76 ppm corresponds to the phenolic proton away from carbonyl group. ^{13}C NMR spectra gives singlet at δ 192.1 ppm due to ketonic carbon C-1 and at δ 178.4 ppm due to enolic carbon C-3 confirming the keto-enol tautomerism in β -diketone **3a**. The IR spectrum showed absorption bands at 3438 (OH), 1743 (C=O) and 1142 cm^{-1} (C-O). The negative test for ester, the presence of characteristic ^1H NMR peaks and ^{13}C NMR peaks are consistent with the structure of 1-(2', 4'-dihydroxy-5'-chlorophenyl)-3-phenyl-propane-1, 3-dione **3a**. The FAB-MS spectrum showed a molecular ion peak at 290 (M^+), confirms the molecular formula $\text{C}_{15}\text{H}_{11}\text{ClO}_4$.

Scheme 1. Synthesis of 1-(2', 4'-dihydroxy-5'-chlorophenyl)-3-aryl-propane-1, 3-diones; (i) Glacial CH_3COOH /anhydrous ZnCl_2 (ii) ArCOOH /Pyridine/ POCl_3 , (iii) NaOH /DMSO.

Antibacterial activity

The synthesized compounds **3a-h** were screened for antibacterial activities against bacteria such as *E. coli*, *P. vulgaris*, *S. aureus*, *B. subtilis* and *P. aeruginosa* using well diffusion method at concentration of $100\text{ }\mu\text{g/mL}$ in acetone. The pure gentamycin, erythromycin and nystatin were used as control. The cultures of above bacterial strains were inoculated in 10 mL nutrient broth and incubated at $37\text{ }^\circ\text{C}$ for 24 h. The petridishes and nutrient agar medium was sterilized by autoclaving. To this sterilized nutrient medium 1 mL of one day old bacterial culture was added and stirred well; this medium was poured into petridishes. The well impregnated with $100\text{ }\mu\text{g/mL}$ of newly synthesized compounds were introduced aseptically in the nutrient agar plate. All the nutrient agar plates were incubated at $37\text{ }^\circ\text{C}$ for 24 h after which the plates were observed for clear zone of inhibition. The screening results indicate

that the compounds **3a-h** showed moderate to excellent antibacterial activities against the selected pathogens Table 3.

Table 3. Antibacterial activity of compounds **3a-h**.

S. No.	Minimum Inhibitory Concentration (MIC) $\mu\text{g mL}^{-1}$				
	Diameter of Inhibition zone, mm				
	Gram-negative			Gram-positive	
	<i>E. coli</i>	<i>P.aeruginosa</i>	<i>P.vulgaris</i>	<i>B. subtilis</i>	<i>S. aureus</i>
3a	44	06	14	05	14
3b	12	--	05	08	11
3c	10	14	07	--	12
3d	07	10	08	13	09
3e	06	18	04	07	--
3f	14	09	19	03	19
3g	06	04	15	--	09
3h	17	07	09	08	16
Std 1	28	22	10	16	10
Std 2	31	19	08	21	07
Std 3	23	21	17	06	11

Minimum Inhibitory Concentration (MIC) 100 $\mu\text{g mL}^{-1}$
Std 1 Gentamycin
Std 2 Erythromycin
Std 3 Nystatin
 -- No zone of inhibition

Conclusion

In the present work various 1-(2', 4'-dihydroxy-5'-chlorophenyl)-3-aryl-propane-1, 3-diones **3a-h** were synthesized by Baker-Venkatraman transformation with NaOH in DMSO and their structures confirmed on the basis of spectral analysis. The ^1H NMR and ^{13}C NMR spectra revealed that the prepared compounds **3a-h** possess characteristic peaks due to the presence of enolic proton (enol form of β -diketone) and phenolic proton adjacent to carbonyl group. These synthesized compounds were screened for in vitro antibacterial activity and found to be promising candidates as new antibacterial agents.

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