SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION AND ANTIMICROBIAL SCREENING OF SOME NEWLY SYNTHESIZED PROPANE-1,3-DIONE (β-DIKETONES) DERIVATIVES

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A simple,efficient and new series of propane-1,3-diones i.e.β-diketone derivatives (4a-d) were prepared via Baker-Venkataraman rearrangement from substituted 2-benzoyloxy acetophenones (3a-d) with potassium hydroxide in pyridine medium and obtained in good yields.The structures of the titled compounds were confirmed by spectral data studies of IR and 1H NMR.The antibacterial and antifungal activity of these newly synthesized compounds (4a-d) were screened by paper disc method and appeared to be significant.

Keywords: 2-Benzoyloxy acetophenones ,Propane-1,3-diones, IR and 1H NMR , Antifungal activity, Antibacterial activity

1.Introduction

Development of simple synthetic steps to widely used organic compounds using readily available of reagents are one of the most important objectives of organic synthesis. In Baker-Venkataraman rearrangement thesynthesis from o-aryloxy acetophenone to β-diketones was utilized. The β-diketones was shows various pharmacological activities like, prophylactic antitumor1, antioxidant2, antisunscreen agents3and biological activity4.The β-diketones have been widely used for the synthesis of heterocyclic compounds such as flavones5,pyrazoles6,2-mercapto pyrimidine7etc.Now recently β-diketones are well known to have keto-enol tautomerism and reported that they have important pharmacophores for the HIV-integrase (1N) inhibitiors8.Substituted propane 1,3-diones are used in various drug containing the heterocyclic moieties, such as isoxazole, carbazole, imidazole and thiazole etc. The β-diketones are used as a ligand in co-ordination chemistry9-10. The synthesis of substituted propane -1,3-diones (β-diketones) are of tremendous important in organic chemistry and medicine, so by focusing on these aspects we are going to synthesized β-diketones asa precursor for different heterocyclic compounds and study their spectroscopic data and antimicrobial properties.

2. Materials and Methods

All solvents and chemicals were of research grade, highest purity and commercially available. The melting points were taken in open capillaries using paraffin Thiele's tube. All the synthesized compounds were purified by recrystallization method. The IR spectra were recorded on Shimadzu IR affinity-1FTIR spectrophotometer in KBr pallets and values were expressed in cm-1.1H NMR spectra were recorded on Bruker Avance II 4000 NMR spectrophotometer in DMSO-d_6 as a solvent and TMS as an internal standard.

3.Synthesis of substituted propane-1,3-diones (β-diketones) (4a-d)

The synthesis involves the following steps.

3.1. General procedure for the synthesis of 4-bromo phenyl acetate (1)

4-bromo phenol (0.05mol) fused with acetic anhydride(5ml) and add sodium acetate. The mixture was refluxed for about 1hr. then cooled for 15 min. and poured in ice crushed water. Acetate layer was separate out by separating funnel and wash several times by water. The product was purified by distillation process to obtained a pure 4-bromo phenyl acetate (1).

3.2. General procedure for the synthesis of5-bromo,2-hydroxy acetophenone (2)

Place anhydrous aluminum chloride (120 g) in kjeldal flask and add 4-bromo phenyl acetate (1) (40 ml) drop wise in a flask. Heat the reaction mixture in oil bath for 60 min at 120^0C temperature. The reaction mixture was cooled and add in to acidified ice crushed water to get crude product. It was purified by dissolving product in acetic acid and decompose in ice cold water to get 5-bromo,2-hydroxy acetophenone (2).

3.3 General procedure for the synthesis of 2-substituted benzoyloxy 5-bromo acetophenone (3a-d)

Place 5-bromo,2-hydroxy acetophenone (2) (0.05mol) and substituted benzoic acid (0.05mol) were dissolved in dry pyridine at 0^0C.Then add $POCl_3$ dropwise with constant stirring bellow 10^0C temperature. The reaction mixture was allowed to stand for overnight at room temperature. The reaction mixture was poured in ice cold acidified 10% HCl. Then the product was wash by 10%$NaHCO_3$ and several times by water. Recrystallized the product by ethanol to obtained a series of 2- substituted benzoyloxy 5-bromo acetophenone (3a-d).

3.4 General procedure for the synthesis of substituted propane-1, 3-diones(β-diketones) (4a-d)

A series of substituted propane-1,3-diones (4a-d) was synthesized by Baker–Venkataraman transformation reaction as shown in **figure 1**. Take 2-substituted benzoyloxy 5-bromo acetophenone (3a-d) (0.05mol) was dissolved in dry pyridine. The reaction mixture was heated up to 60^0C and add pulverized KOH slowly with constant stirring. After 5-6 hr. the reaction mixture was acidified by dil. HCl (1:1) in ice cold water. The crude product was filtered, washed with $NaHCO_3$(10%) and several times by water. Recrystallized the product from ethanol-acetic acid mixture to get substituted propane 1,3-diones (β-diketones) (4a-d) having good yield as shown in **table1**

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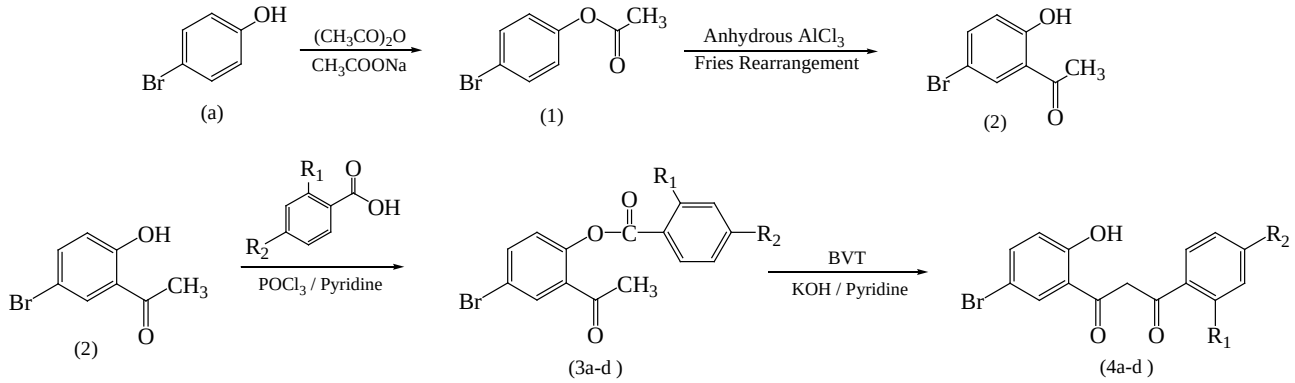
Figure 1. Scheme for the synthesis of substituted propane-1,3-diones (β-diketones) (4a-d)



R_1 – H, Cl R_2 - CH_3, NO_2, H, Cl.

4. Spectral data of all substituted propane -1,3-diones(4a-d)

4.1: 1-(5'-bromo-2'-hydroxy phenyl)-3-(4'-methyl phenyl) propane-1,3-dione(4a)

Solid, dark yellow colour, IR (KBr): 3335 cm^{-1}(Phenolic -OH stretch),3034 cm^{-1}(Aromatic C-H stretch), 2945 cm^{-1}(Aliphatic C-H stretch),1690 cm^{-1}(C=O stretch),1505 cm^{-1}(Aromatic C=C stretch).^{1}H NMR (DMSO-d_6): δ 4.8 (S,1H of OH), δ 2.5 (S, 3H of CH_3), δ 3.44 (S, 2H of CH_2), δ 7.2-8.12(m,7H of Ar C-H).

4.2: 1-(5'-bromo-2'-hydroxy phenyl)-3-(4'nitrophenyl) propane-1,3-dione(4b)

Solid dark yellow colour, IR (KBr):3388 cm^{-1}(Phenolic -OH stretch), 2918 cm^{-1}(Aromatic C-H stretch), 2858 cm^{-1} (Aliphatic C-H stretch),1652 cm^{-1}(C=O stretch),1564 cm^{-1}(Aromatic C=C stretch),1377 cm^{-1}(C-N stretch).^{1}H NMR (DMSO-d_6): δ 6.7 (S, 1H of OH), δ 3.36 (S, 2H of CH_2), δ 6.85-8.30 (m, 7H of Ar C-H).

Table 1 – Physical data of substituted propane-1,3-dione (β-diketones) (4a-d).

Entry	Compound Code	R_1	R_2	M.F.	M.W.	M.P. (^oC)	Yield%
1	4a	H	CH_3	$C_{10}H_{13}BrO_3$	335.18	154-156	72 %
2	4b	H	NO_2	$C_{15}H_{10}B_rNO_5$	364.15	190-192	68%
3	4c	Cl	H	$C_{15}H_{10}BrClO_3$	353.6	112-114	70%
4	4d	H	Cl	$C_{15}H_{10}BrClO_3$	353.6	114-116	74%

M.F.-Molecular formula, M.W.-Molecular weight, M.P.-Melting points

4.3: 1-(5'-bromo-2'-hydroxyphenyl)-3-(2'chlorophenyl) propane-1,3-dione(4c)

Solid dark brown colour,IR (KBr): 3300 cm^{-1} (Phenolic -OH stretch), 3131 cm^{-1}(Aromatic C-H stretch), 2918 cm^{-1} (Aliphatic C-H stretch), 1703 cm^{-1} (C=O stretch),1559 cm^{-1}(Aromatic C=C stretch),766 cm^{-1}(C-Cl stretch).^{1}H NMR (DMSO-d_6): δ 3.53 (S, 1H of OH), δ 2.63 (S, 2H of CH_2), δ 6.92-8.19 (m,7H of Ar C-H).

4..4: 1-(5'-bromo-2'-hydroxyphenyl)-3-(4'chlorophenyl) propane-1,3-dione(4d)

Solid dark yellow colour,IR (KBr): 3310 cm^{-1} (Phenolic -OH stretch), 3124 cm^{-1} (Aromatic C-H stretch), 3042 cm^{-1} (Aliphatic C-H stretch), 1733 cm^{-1} (C=O stretch), 1558 cm-1(Aromatic C=C stretch), 709 cm^{-1}(C-Cl stretch). ^{1}H NMR (DMSO-d_6): δ 4.76 (S, 1H of OH), δ 3.87 (S, 2H of CH_2), δ 6.97-8.11 (m, 7H of Ar C-H).

5.Antimicrobial activity

5.1 Antibacterial Activity

The Synthesized substituted propane-1,3-diones (β-diketones) (4a-d) was screened by antibacterial activity against gram +ve *Staphylococcus aureus* and gram –ve *Salmonella typhi* bacteria by paper disc method[11].The compounds 4a-d was tasted at 50 µg/ml,100 µg/ml and 250µg/ml of concentration in DMSO solvent in which sterile filter paper disc was dipped. Dried the disc and placed the nutrient ager plates spreaded with bacteria. After 24 hr. of incubation at 37^0C the dimeter of zone of inhibition were measured in mm by metric ruler scale and compared with standard ampicillin at 25 µg/ml concentration as antibiotic drug. The results of screening are given in **table 2**.

Table 2 - Antibacterial activity of substituted propane-1, 3-dione (4a-d)

Zone of inhibition (in mm) at µg/ml concentrations							
Entry	Compound Codes	*Staphylococcus aureus* (Gram +ve)			*Salmonella typhi* (Gram –ve)		
		50	100	250	50	100	250
1	4a	--	--	--	--	--	--
2	4b	9.0	7.0	8.0	--	--	--
3	4c	9.0	6.0	7.0	--	--	--
4	4d	8.0	8.0	14.0	7.0	7.0	7.0
5	Std.	24.0	24.0	24.0	24.0	24.0	24.0
6	Control	--	--	--	--	--	--

Std.-Ampicillin, Control-DMSO Solvent," -- "denoted No zone of inhibition

5.2 Antifungal Activity

The synthesized substituted propane-1,3-diones (β-diketones) (4a-d) was also screened for antifungal activity against *candida albican* and *aspergillus niger* by using paper disc method at 50 µg/ml,100 µg/ml and 250 µg/ml concentration in DMSO solvent. The zone of inhibition was measured in mm scale. The antifungal activity of the synthesized compounds was compared with standard Fluconazole at 25 µg/ml concentration as an antibiotic drug. The result of antifungal data was found to be very poor. The β-diketones (4a-d) does not show any zone of inhibition.

Result and Discussion

A series of substituted propane-1,3-diones(β-diketones) (4a-d) was synthesized by Baker–Venkataraman transformation to get good yield. Among the all compounds 4b,4c and 4d shows comparatively better zone of inhibition than 4a against *Staphylococcus aureus*(*Gram +ve)*and 4d show good activity than 4a,4b and 4c against *S. typhi* (Gram –ve). The observed data of antifungal activity were found to be inactive. Compound 4a,4b,4c and 4d does not shows any zone of inhibition at any concentration.

Conclusion

In the present work newly synthesized substituted propane-1,3-diones (β-diketones) (4a-d) involves different steps to get good yield in a short time period. The structure of β-diketones was elucidated on the basis of ^{1}H NMR and IR spectral data. In antibacterial activity only compound 4b,4c and 4d shows zone of inhibition against *s. aureus*. The only compound 4d shows zone of inhibition against *s. typhi*. The result of antifungal activity is negative in which compound 4a-d does not show any zone of inhibition against *candida albican* and *aspergillus nigar*. We are continuing our research work in extending of β-diketones (4a-d) for further synthesis of hetero cyclic compounds

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