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**Archives of Applied Science Research, 2012, 4 (4):1839-1843**
*(http://scholarsresearchlibrary.com/archive.html)*

**ISSN 0975-508X**
**CODEN (USA) AASRC9**

# Synthesis and Characterization of β -Diketone Ligands and Their Antimicrobial Activity

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**ABSTRACT**

*A new β-diketone ligands derived from 2- hydroxy acetophene and 3,4,4-triethoxy benzoic acid have been synthesized. The ligand was characterized by elemental analysis, conductometry, UV-visible, IR spectra, [1]H-NMR and [13]C-NMR. IR spectral data suggest that the ligand behaves as a monobasic bidentate ligand with (O:O) donor. The β-diketone ligands were screened for antibacterial activity against Pseudomonas Aeurogenosa and Escherichia coli and fungicidal activity were tested against Aspergillus Niger and Trichoderma.*

**Keywords:** β-diketones, antibacterial, fungicidal activity.

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## INTRODUCTION

β-diketones are among the most widely used ligands in co-ordination chemistry[1-2]. These compounds can exist in solution as well as in solid as keto and enol tautomers. Since the enolic hydrogen is labile, it can be replaced by a metal cation to form a six membered chelate ring. The β-diketonate complexes thus formed have been the topic of hundreds of papers and reviews[1-4]. The research being stimulated by the versatility of these compounds as NMR shift reagents[5], laser chelates[6], extraction agents[7], chemical and photochemical catalysts[8] as well as their biological activities as evidenced from their anticancer[9], anti-tumor[10], anti-oxidant[11], anti-inflammatory[12], anti-viral[13] and immunomodulatory activities[14]

The synthesis and characterization of β-diketones is of tremendous importance. By focussing on these aspects and earlier research on biologically active of ortho hydroxy acetophenone containing β-dicarbonyl moieties, we are reporting in this communication, synthesis, spectral and biological studies of β-diketone.

## MATERIALS AND METHODS

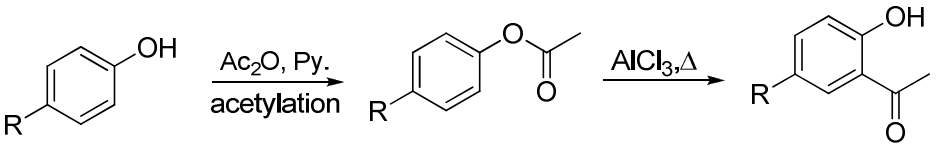
### Experimental

Micro analysis of the ligand are performed at the Central Drug Research Institute (CDRI), Lucknow (India). The $^1$H NMR spectra of ligand was recorded on EM-360 spectrophotometer at RSIC, Punjab University, Chandigarh (India). IR spectra of ligand were recorded in KBr pellet on a FTIR-4100 Jasco in the region 4000-400 cm$^{-1}$.

**Synthesis and Characterization of β-diketones**
The method used for synthesis of diketones involves two steps.

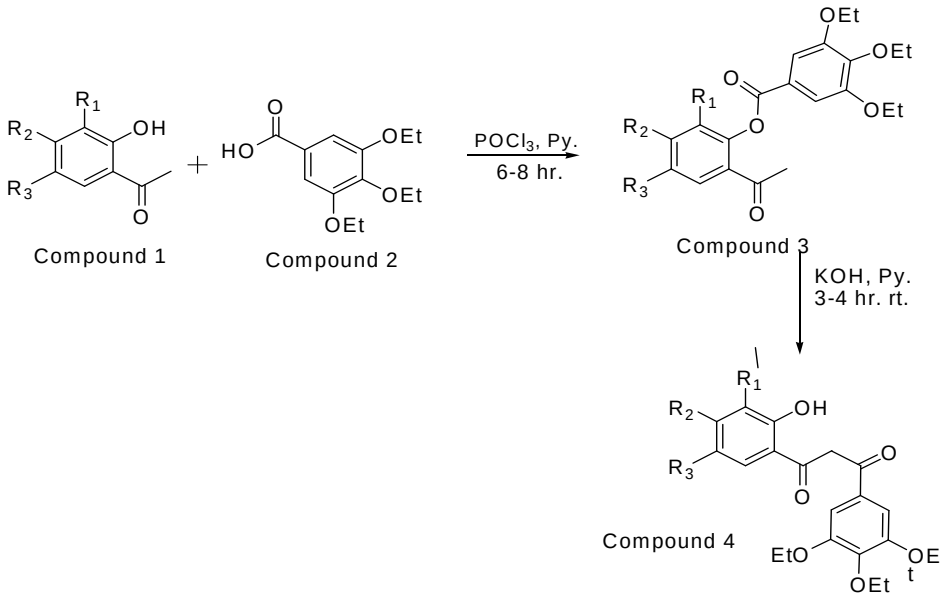
**Synthesis of 2- Hydroxy Acetophenone:**
The equimolar quantities of substituted phenol and acetic anhydride were taken in to 500ml round bottomed flask and 5ml pyridine was added. The reaction mixture was kept overnight and then it was poured in to crushed ice, thus two layers were formed in which upper layer contains ester, separated by separating funnel and washed with distilled water for two to four times followed by 2% NaOH solution .

The obtained pure ester was subjected to Fries rearrangement. Ester (1mol) was slowly added in powdered anhydrous aluminum chloride (1-5mol). The mixture was heated in an oil bath for one and half hour and allowed to cool. The mixture was then kept overnight in crushed ice with 5-6 drops of concentrated HCl to form precipitate. It was separated by filtration and recrystallised by minimum quantity of ethanol to obtain pure product. Same procedure was used for the synthesis of other 2-hydroxy acetophenones.




**Synthesis of β-diketones:-**
1, 3 diketones were obtained by the reaction of substituted 2- hydroxy acetophene with 3,4,4-triethoxy benzoic acid in pyridine and $POCl_3$ at room temperature. The ester obtained (1) was converted into 1,3 dione(2) by the Baker-Venkataraman rearrangement.

Equimolar amount of compounds 1 and 2 were dissolved in 50ml dry pyridine. The reaction mixture was then cooled to 0°C and (0.06 mol) phosphorus oxychloride was added drop wise maintaining temperature below 10°C. The reaction mixture was kept over night at room temperature. It was then poured on crushed ice with vigorous stirring. The crimson coloured solid ester obtained was filtered and washed several times with ice-cold water. Ester (3) was then crystallized with distilled ethanol. Purity of compound was checked by TLC. 0.03 moles ester (Compound 3) was dissolved in 15ml of dry pyridine. To this, powdered KOH (1gm) was added and the reaction mixture was stirred on magnetic stirrer at room temperature for 3 hours. It was then poured over crushed ice and acidified with concentrated HCL. Thus obtained Yellow coloured product (compound4) was recrystallized from ethanol




**Scheme-1**

(Yield 50-55%). Purity of all synthesized β-diketones was checked by TLC using silica gel and melting points. The overall reaction is presented inscheme1.

**Antimicrobial activity**

The antibacterial activity of free ligands and control (DMF solvent was tested in vitro against gram +ve bacteria (*Pseudomonas Aeurogenosa)* and gram –ve bacteria *(E.Coli)* by paper disc method [15]. Sterile (10mm) diameter Whatmann No. 42 paper discs were soaked in different concentrations of the ligand (250ppm and 500ppm) in DMF, dried and then placed on the lawn culture of nutrient agar plates. The plates were then incubated for 24h at 37 ºC and the inhibition zone around each disc was measured. The results obtained were compared with known antibiotics, Ciprofloxin (TABLE V). Three replicates were taken and average value is given.

The ligand and control were screened for antifungal activity against the fungi *Aspergillus niger* and *Trichoderma* at 250ppm and 500ppm levels respectively by mycelia dry weight method The culture of fungi were purified by single spore isolation technique. The glucose nitrate (GN) medium was used for the growth of fungi. The mycelial biomass was then dried along with filter paper in an ovean at 65±5 ºC to constant weight, cooled and finally weighed. The mycelial dry weight (MDW) was obtained by subtracting the weight of mycelium free filter paper from final dry weight [16]. Three replicates of each treatment were repeated in all experiments. The MDW was corrected each time by subtracting the dry weight obtained from incubated flask under similar experimental conditions. The yields of MDW in mg are presented in (TABLE VI). The percentage error was found to be ± 0.01. The percent decrease in mycelia dry weight to the test compound in each case was calculated and tabulated in terms of average percentage inhibition. The results indicate that the ligand and its metal complexes arrested the growth of fungi.

## RESULTS AND DISSCUSSION

**Characterization of ligands**:-

All synthesized ligands were stable to air and moisture. Soluble in ethanol, methanol, chloroform, dichloromethane and insoluble in water and ether. The structural features of ligands were elucidated with the help of elemental analysis.

**Table:-1 Physical and analytical data of β- diketones**

| Ligand | R | | | M. F (M. W.) | M.P. °C | Yield (%) | Colour | % Found (Calcd.) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $R_1$ | $R_2$ | $R_3$ | | | | | C | H | Cl | *Br* |
| $L_1$ | H | H | H | $C_{21}H_{24}O_6$ (372) | 89-90 | 65% | Yellow | 67.77 (67.74) | 6.40 (6.45) | - | – |
| $L_2$ | H | H | $CH_3$ | $C_{22}H_{26}O_6$ (386) | 120-122 | 72% | Yellow | 68.34 (68.39) | 6.77 (6.73) | – | – |
| $L_3$ | H | $CH_3$ | Cl | $C_{22}H_{25}O_6Cl$ (420) | 131-132 | 75% | Yellow | 62.91 (62.85) | 5.99 (5.95) | 8.39 (8.33) | – |
| $L_4$ | H | H | Cl | $C_{21}H_{23}O_6Cl$ (407) | 135-136 | 70% | Yellow | 61.96 (61.91) | 5.21 (5.15) | 8.62 (8.59) | – |
| $L_5$ | H | H | Br | $C_{21}H_{23}O_6Br$ (452) | 128-130 | 68% | Yellow | 55.78 (55.75) | 5.10 (5.08) | - | 17.72 (17.69) |

One reprsentive ligand *1-(5-bromo-2-hydroxyphenyl)-3-hydroxyl-3-(3,4,5triehoxyphenyl) prop-2-en-1-one was scanned for IR*, $^1$H nmr, $^{13}$Cnmr and mass spectrum. Following are the scanning results are given below.

**IR Spectral studies**

**IR(cm-1) (KBr) spectral data of compound:**

3498 cm-1 (hydroxyl moiety), 2945 cm-1 Aliphatic symmetrical streteching) , 2908 cm-1(Asymmetrical stretching)

**$^1$H NMR spectral studies**

$^1$HNMR (CDCl3) spectral data of compound

1.43 δ ppm (t, 9H, -$CH_3$ group), 4.19 δ ppm (q, 6H, -Ch2 group), 6.63-7.84 δ ppm (5H, from aromatic ring), 12.05 δ ppm (s, Phenolic –OH), 15.76 δ ppm (s, Enolic –OH).

**$^{13}$CNMR Spectra**

**$^{13}$C** NMR (CDCl3) spectral data of compound (50 MHz, $CDCl_3$, δ / ppm) of the ligand, shows peaks at 14.86, 65.12, 91.62, 105-153, 178.84, 193.43.

**Mass Spectral Studies**

Mass spectrum were found to match with the theoretical expected values as $ES^-$ peak observed at 449.2 with 100% and $ES^+$ value was matched with 451.1 with 100% abundances.

**Antifungel Activity**

The percentage of inhibition of growth of both fungi due to ligand was found to be in the order $L_1 > L_2 > L_4 > L_5 > L_3$. The probable correlation between structure and activity can be established, that the presence of halogen, hydroxy and ethoxy group in the ligand moiety enhances fungal toxicity. It is suggested that the compound having antimicrobial activity may act either by killing the microbes or inhibiting the multiplicity of microbes or blocking their active sites

**Antibacterial Activity**

It can be seen that the ligands show weak to moderate activity with 10- 18 mm zone of inhibition at 500 ppm and 12 – 22 mm zone of inhibition at 1000 ppm concentration for both the organisms. Standard drug Ciprofloxacin showed very high activity with 27-30 mm zone of inhibition at 500 ppm and 34-38 mm at 1000 ppm concentration under the same conditions. The probable correlation between structure and activity can be established, that the presence of halogen, hydroxy and ethoxy group in the ligand moiety increases toxicity towards bacteria. Inhibition activity of ligand may be attributed due to either by killing the microbes or inhibiting the multiplicity of microbes or blocking their active sites.

**Table 2. Yield of Mycelial Dry Weight (MDW) in mg(% of inhibition)after 168hrs.**

| Ligand | ***Aspergillusniger*** | | ***Trichoderma*** | |
|---|---|---|---|---|
| | **250ppm** | **500ppm** | **250ppm** | **500ppm** |
| Control | 55 | 55 | 62 | 62 |
| L1 | 48(12.72 ) | 35(36.36 ) | 56(9.62 ) | 45(27.41 ) |
| L2 | 42( 23.62) | 31( 43.63) | 45( 27.41) | 34( 45.16) |
| L3 | 36( 34.54) | 25( 54.54) | 42( 32.25) | 31( 50) |
| L4 | 41( 25.45) | 33( 40) | 47( 24.19) | 36( 41.95) |
| L5 | 40( 27.27) | 31( 43.63) | 47(24.19 ) | 35( 43.54) |

**Table 3. Antibacterial activity of ligands**

| **Test Compound** | **Diameter of inhibition zone (mm)** | | | |
|---|---|---|---|---|
| | **E. Coli** | | **Pseudomonas Aeurogenosa** | |
| | 500 ppm | 1000 ppm | 500 ppm | 1000 ppm |
| Ciprofloxacin | 27 | 34 | 30 | 38 |
| $L_1$ | 13 | 15 | 18 | 22 |
| $L_2$ | 12 | 14 | 15 | 19 |
| $L_3$ | 10 | 12 | 11 | 14 |
| $L_4$ | 11 | 14 | 14 | 17 |
| $L_5$ | 11 | 14 | 13 | 15 |

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