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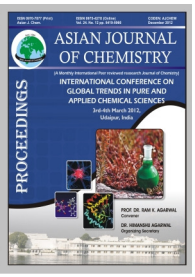

Synthesis and Biological Evaluation of Some 3,5-Dibromo-4-hydroxy Enoness†

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Enones having an α,β-unsaturated carbonyl systems are important as Michael acceptors and constitute an important class of biologically active compounds. Enones are one of the most versatile synthons for various chemical transformations leading to the synthesis of several biodynamic heterocyclic compounds. Therefore, the chemistry of synthetic enones is most dynamic and challenging area embracing a vast spectrum of advances of both theoretical and practical relevance. In view of this, in the present paper synthesis of some 3,5-dibromo-4-hydroxyphenyl enones are reported along with their herbicidal, fungicidal, insecticidal, animal health and antibacterial activities. Some of the compounds showed promising biological activities.

Key Words: Synthesis, Enones, Biological activities.

INTRODUCTION

Chalcones are the biogenetic precursors of all known flavonoids and are abundant in edible plants and chemicals. Chalcone is *trans*-1,3-diphenylpropenone in which two aromatic rings are joined by a three carbon α, β-unsaturated carbonyl system, commonly known as enones. They are 1,3-diphenyl enones and are important Michael acceptors. Depending on the substitution pattern on the two aromatic rings a wide range of pharmacological activities have been cited for various 1,3-diphenyl enones. These include antiinflammatory[1], antioxidant[2], antiviral[3], antibacterial[4], antileishmanial[5], K^+ channel inhibitor[6], antimalarial[7] and as antituberculotics[8]. Phenolic ketones bearing halogen in the nucleus are of diverse biological interest. *p*-Hydroxyacetophenone bearing halogen substituents in the 3- and 5- position are structurally related to antagonist tyroxine[9]. Prompted by these finding and in continuation to our interest in the synthesis of biodynamic chalcones[10], in the present work it was thought to incorporate 3,5-dibromo-4-hydroxy phenyl nucleus in the molecular framework of enones by condensing 3,5-dibromo-4-hydroxy acetophenone (I) with different substituted aromatic aldehyde in the presence of base. The resulting 1,3-diphenyl enones (chalcones) were characterized by their colour test, elemental analysis, IR, ^{1}H NMR and mass data. These compounds were also screened for their antibacterial, herbicidal, fungicidal, insecticidal and animal health activity.

EXPERIMENTAL

Melting point were determined in open capillaries are uncorrected. IR spectra (KBr) were recorded on a Perkin-Elmer 1800 (FTIR) spectrometer, PMR spectra ($CDCl_3$) on a Perkin-Elmer R-32 (90 MHz) spectrometer and mass spectra on a Jeol D-300 (El/Cl) spectrometer. Purity of the compounds was checked by TLC. 3,5-Dibromo-4-hydroxyacetophenone(II) was prepared by reported method m.p. 180 ºC (lit.[9] m.p. 181 ºC).

Preparation of 3',5'-dibromo-4'-hydroxy chalcones (V a-h): To a solution of 3,5- dibromo-4-hydroxy acetophenone (0.1 mol)in ethanol (50 mL), an appropriate aromatic aldehyde (0.1 mol) was added. To this mixture aqueous sodium hydroxide (50 %, 10 mL) was poured gradually while stirring. The mixture was kept at room temperature for 5 h. The sodium salt of chalcone separated was decomposed by ice cold hydrochloric acid (50 %, 40 mL). The separated chalcone was filtered and washed with water (2 × 50). It was recrystallized from ethanol to afford analytical samples. The characterization data have been tabulated in Table-1.

RESULTS AND DISCUSSION

p-Hydroxyacetophenone(I) on treatment with bromine in aqueous acetic acid resulted 3,5-dibromo-4-hydroxy acetophenone(II) in good yield. Claisen-Schmidt condensation of 3,5-dibromo-4-hydroxy acetophenone(II) with different substituted aldehydes(III) in presence of base resulted 3',5'-

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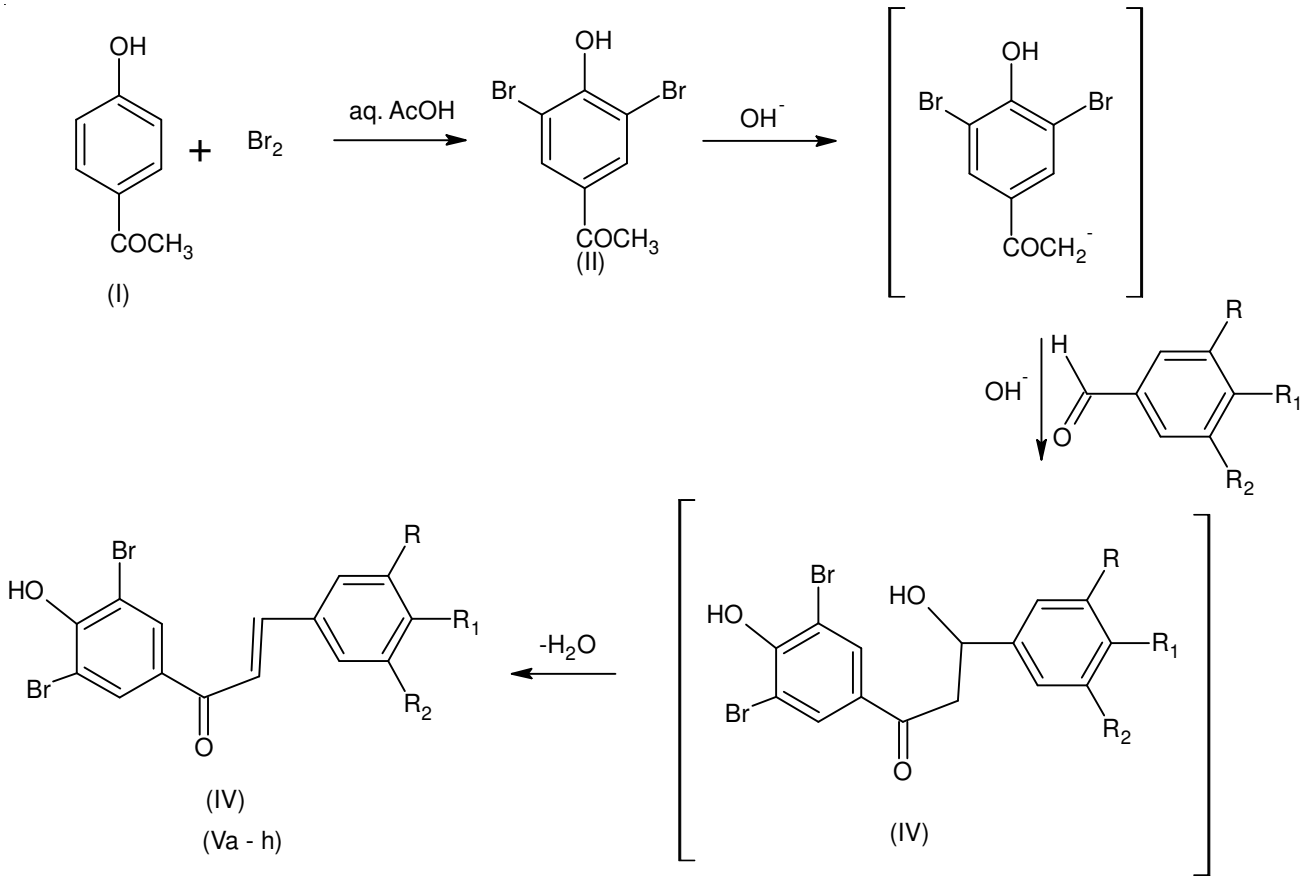
TABLE-1
CHARACTERIZATION DATA OF COMPOUNDS (Va-h)

Comp. no.	R	R_1	R_2	m.f.	Yield (%)	m.p.* (°C)	Found (%) (cal.)		
							C	H	N
Va	H	H	H	$C_{15}H_{10}O_2Br_2$ (382.069)	50	161	47.27 (47.15)	2.58 (2.68)	–
Vb	H	Cl	H	$C_{15}H_9O_2Br_2Cl$ (416.514)	64	148	43.28 (43.26)	2.29 (2.18)	–
Vc	H	H	NO_2	$C_{15}H_9NO_4Br_2$ (427.066)	70	268	42.31 (42.19)	2.17 (2.12)	3.36 (3.28)
Vd	H	NO_2	H	$C_{15}HNO_4Br_2$ (427.066)	72	262	42.22 (42.19)	2.15 (2.12)	3.32 (3.28)
Ve	H	OCH_3	H	$C_{16}H_{12}O_3Br_2$ (412.096)	53	168	46.82 (46.64)	2.98 (2.94)	–
Vf	H	OCH_3	OCH_3	$C_{17}H_{14}O_4Br_2$ (442.127)	71	100	46.25 (46.18)	3.25 (3.09)	–
Vg	OCH_3	OCH_3	OCH_3	$C_{18}H_{16}O_5Br_2$ (427.148)	50	264	50.72 (50.68)	3.50 (3.78)	–
Vh	H	CH_3	H	$C_{16}H_{12}O_2Br_2$ (396.092)	71	171	48.72 (48.52)	3.01 (3.05)	–

*All the compounds were recrystallized in ethanol.



Scheme-I

dibromo-4'-hydroxy substituted chalcones (**Va-h**) in 50-75 % yield (Scheme-I). These compounds were recrystallized as orange, yellow or pale yellow crystalline solid using ethanol as solvent. The characterization of compounds (**Va-h**) has been carried out by elemental analysis,UV, IR, ^{1}H NMR, mass spectral studies (Tables 1 and 2).

Substituted chalcones (**Va-h**) when wetted with concentrated conc. H_2SO_4 and conc. H_2SO_4 + cons.HNO_3 showed change in colour. This phenomenon of colour change is known as halochroism. This colour change has been shown in Table-3.

Spectral studies: Conjugation in chalcone molecule give dominant UV absorption band I at 300-400 nm. In the present cases (**Va-h**) increased oxygenation of A and B ring resulted bathochromic shift (410-420) particularly in the position band I. In the IR spectra of compounds (**Va-h**) characteristic absorption at 3248-3200 cm^{-1} ν(OH), 1645-1640 cm^{-1} ν(>C=O), -3180 ν(Ar-H), 1590-1450 ν(skeletal C-C) and 900-700 cm^{-1} (substituted phenyl) were observed, CH deformation frequencies characteristic of the *trans* ethylenic groups were found in the regions 1350-1250 cm^{-1} and 1000-950 cm^{-1}.

The proton NMR spectrum showed doublets around δ 7.60 (C_α-H) and δ 7.84 (C_β-H) with coupling constant value of 15 Hz indicated the presence of vinylic hydrogen in E-configuration. A multiplet at δ 6.94-7.18 for ring B protons and around δ 7.4 for ring A protons were observed. Singlet at δ 8.22 was observed due to phenolic proton at 4'-OH. Characterization of mass spectral studies revealed the presence of strong ion for M^+, $[M-H]^+$ and $[M-CO]^+$. Detail spectral data are given in Table-2.

Antibacterial activity: Synthesized compounds (**Va-h**) were screened for their antibacterial activity at 250 µg/mL concentration in ethanol against Gram positive organisms *Streptococcus viridans* and *Staphylococcus aureus, Streptococcus*

pyogenes and Gram negative organism *Escherichia coli*. The paper disc method was used for this evaluation[11]. The results of antibacterial activity have been tabulated in Table-4.

Herbicidal activity: Compounds were tested both pre and post emergence against 18 economically important weeds and crops in an 80 ± 0.2 % acetone solution. Pre emergence and post emergence treatment were evaluated at 3 and 2 weeks after treatment respectively. The minimum sample used in this test was 250 mg. The results of herbicidal activity of synthesized compounds are tabulated in Table-4. All the synthesized compounds were found inactive in their insecticidal, fungicidal and animal health screen.

TABLE-2
UV, IR, 'H NMR* AND MASS SPECTRAL DATA OF COMPOUNDS (Va-h)

Comp No.	UV (C_2H_5OH)		IR(KBr) (cm^{-1})	Mass (m/z)		
	λ_{max} (mμ)	O.D.		$[M]^+$	$[M+2]^+$	$[M+4]^+$
Va	385	1.415	1655	382	384	-
Vb	405	1.305	1658	416	418	420
Vc	420	1.509	1645	-	-	-
Vd	370	1.371	1648	-	-	-
Ve	410	1.691	1645	412	414	-
Vf	410	1.673	1648	442	444	446
Vg	410	1.664	1645	-	-	-
Vh	400	1.525	1645	396	398	-

*'H NMR spectra of comp. $CDCl_3$; δppm (Va) 6.94-7.40 (m, 7H, Ar-H), 7.60 (d, 1H, α-H), 7.84 (d, 1H, β-H) and 8.22 (s, 1H, OH)
(Ve): 3.86 (s, 3H, $-OCH_3$), 6.94-7.86 (m, 6H, Ar-H), 7.60 (d, 1H, α-H), 7.84 (d, 1H, β-H) and 8.22 (s, 1H, OH)
(Vf): 3.94 (s, 3H, $-OCH_3$), 3.97 (s, 3H, $-OCH_3$), 6.88-7.3 (m, 5H, Ar-H), 7. 70 (d, 1H, α-H), 7.8 (d, 1H, β-H) and 8.22 (s, 1H, OH)

TABLE-3
HALOCHROISM BY 3',5'-dibromo-4'-hydroxy chalcones (Va-h)

Comp. no.	Original colour	Change in colour	
		Conc. H_2SO_4	Conc. H_2SO_4 + cons. HNO_3
Va	Yellow	Red	Yellow
Vb	Pale Yellow	Dark Purple	Light Yellow
Vc	Pale Yellow	Yellow	Orange
Vd	Pale Yellow	Yellow	Orange
Ve	Orange	Blood Red	Orange Red
Vf	Cream	Blood Red	Light Yellow
Vg	Yellow	Purple Red	Light Orange
Vh	Yellow needles	Red	Light Yellow

TABLE-4
SCREENING RESULTS OF ANTIBACTERIAL AND HERBICIDAL ACTIVITY

Comp No.	Antibacterial (Zone of inhibition mm)		Herbicidal activity
	S. aureus	*S. pyogenes*	
II	20	-	-
Va	11	11	-
Vb	13	12	Moderate
Vc	-	12	-
Vd	-	11	-
Ve	20	13	Moderate
Vf	12	14	-
Vg	-	-	-
Vh	18	11	

Note: All synthesized enones (Va-h) were found inactive against S.*viridance, E. coli*., insectisidal, fungicidal and animal health activity

Conclusion

Enones having 3'5'-dibromo-4'-hydroxyphenyl group along with 4-OCH_3/CH_3 substituent in ring B compounds **Ve** and **Vh** have shown promising antibacterial activity against *S. aureus* where as enones Vb and Ve having 4-Cl or 4- OCH_3 in ring B emerged as potential herbicidal agents.

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