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SYNTHESIS OF SOME NEW BIO ACTIVE PHTHALIDES AND THEIR ANTIBACTERIAL ACTIVITY

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Synthesis of some bioactive phthalides have been reported. Structure of these phthalides have been established on the basis of elemental analysis, IR and NMR spectral data. These phthalides have been evaluated for their antibacterial activity against the bacteria *S. aureus* and *E. coli.*

INTRODUCTION

In the continunation of our previous work [1-9] we synthesise some new biologically active analogues of phthalein dyes which have been screened for their antibacterial property. The synthesised compounds are unsymmetrically substituted phthalides [I-V], in which the central triphenylmethane carbon is attached to two different phenyl rings. Antibacterial activity of these phthalides has been tested against the two bacteria *Staphylococcus aureus* and *Eschehchia Coli.*

Phthalide I, was obtained by the reaction of 2-(Methyl-5-isopropylbenzoyl) benzoic acid with resorcinol in presence of conc. H_2SO_4. Acetylation, bromination, iodination and mercuration of I gives the phthalides II, III, IV and V respectively. In the present study the synthesis and purification of phthalides [I-V] were carried out by the procedure reported for similar compounds in our earlier communication [1].

(I) 3-(2-Methyl-5-isopropylphenyl)-3-(2, 4-dihydroxyphenyl) phthalide.

(II) 3-(2-Methyl-5-isopropylphenyl)-3-(2, 4-diacetoxyphenyl) phthalide.

(III) 3-(2-Methyl-5-isopropylphenyl)-3-(3, 5-dibromo-2, 4-dihydroxyphenyl) phthalide.

(IV) 3-(2-Methyl-5-isopropylphenyl)-3-(3, 5-diiodo-2, 4-dihydroxyphenyl) phthalide.

(V) 3-(2-Methyl-5-isopropylphenyl)-3-(3, 5-diacetoxymercuri-2, 4-dihydroxyphenyl) phthalide.

EXPERIMENTAL

Structures of these compounds [I-V] have been established on the basis of elemental analysis, IR and NMR spectral data. Purity of the products were checked by TLC. Process of Acetylation, bromination, iodination and mercuration of I, gives the phthalides, II, III, IV and V respectively.

Physical and analytical data of the synthesised products are given in Table-1.

Phthalides	Colours	Yield (%)	MP (°C)	Mol. Formula	*v* max (cm^{-1})
I	Pale yellow	83.3	125-126	$C_{24}H_{22}O_4$	3423, 1736, 758, 694
II.	Yellowish brown	88.3	108-110	$C_{28}H_{26}O_6$	-,1773, 758, 695
III	Yellowish orange	55	120-122	$C_{24}H_{20}O_4Br_2$	3420,1780,760,694
IV	Brick red	70	129-130	$C_{24}H_2o04l_2$	3423,1769,758,696
V	Pinkish orange	64.1	>280	$C_{28}H_{26}O_8Hg_2$	3448, 1747,1559,1412,762,695

Antibacterial screening

All compounds [I-V] were tested for their Antibacterial property against two bacteria by paper disc diffussion method [10]. The two bacteria tested are *Staphylococcus aureus* and *Escherichia Coli.* The media for antibacterial activity was prepared by adding 2% agar to the oxoid nutrient medium. The sterilised discs soaked thoroughly in the solution of the compounds (4% in chloroform) were pressed over the seeded media petridishes and incubated at 30°C for 24 hours. The experiments were also performed with standard antibacterial (4% Gentamycin and 4% Tetracycline) under the same conditions. The activities of the phthalides are compared with standard drugs, results of activity are presented in Table-2.

Table-2 : Antibacterial activity of phthalides (I-V) and reference compounds

Phthalides	Zone of inhibition in mm	
	S.aureus	***E.Coli***
I	+	+
II	+	++
III	+	+++
IV	+++	++++
V	++++	++++
Standard, Gentamycin	++++	++++
Tetracycline	++++	++++

(+ +) Slightly active, (+ + +) Moderately active and (+ + + +) Highly active.

Results and discussion

IR spectra (in KBr, v max in cm^{-1}) of phthalides [I and III-IV] displayed a broad and strong absorption band in the region 3448-3420 due to OH stretching vibrations. The diacetyl derivative [II] exhibited a band at 1773 (CO of phenolic acetate). All phthalides [I-V] showed a sharp and strong band at 1780 to 1736 which is characteristic of lactonic carbonyl group. Presence of this band is a significant evidence in favour of the proposed lactonic structures. The spectra of all the dyes showed one intense band at 762-758 and a weaker band at 696-694 both of which are characteristic of an o-disubstituted phthalein ring [l1]. In phthalide V, two strong peaks noticed around 1559 and 1412 can be ascribed to asymmetric and symmetric carbonyl stretching vibrations respectively of $HgOCOCH_3$ groups. In PMR spectra (in DMSO-d_6 chemical shifts in 8 Scale) of phthalide I, a singlet of phenolic hydroxyl protons

appeared near 9.5 (s) ppm, the aromatic protons appeared as a multiplet in the region between 6.5 and 8.2 ppm. Methyl protons and methine proton associated with isopropyl group gave a doublet at 1.2 ppm and heptet at 2.5-3.7 ppm respectively, while the protons of the methyl group directly attached with benzene ring appeared as a singlet at 2.2 ppm.

Antibacterial Activity

Results of antibacterial screening of phthalides [I-V] and standard drugs have been given in Table-2. A critical examination of the activity clearly indicates that mercurated compound [V] was found to be as active as standard drugs. Diiodo compound [IV] was also highly active in case of *E.coli,* but moderately active in case of *S.aureus.* The phthalide III was also highly active against bacteria *E.coli.* Remaining phthalides were slightly active.

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