SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF – 5 – (SUBSTITUTED PHENYL) – 5 – (SUBSTITUTED BENZYL) – 2 – SUBSTITUTED THIOHYDANTOIN.

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Abstract:

2-hydroxy-3-substituted acetophenone were refluxed in DMSO medium in presence of mercuric acetate to get substituted coumaran-3-ones. The resulting substituted coumaran-3-ones is refluxed with thiourea in alkaline medium and alcohol gives 5-(substituted phenyl)-5-(substituted benzyl)-2-substituted thiohydantoin, which show strong antibacterial and antifungal activity. The identities of these compounds have been established on the basis of usual chemical transformation and IR, NMR spectral studies and all the compounds are screened for their antimicrobial activity.

Keywords:

Synthesis, Substituted coumaran-3-one, thiourea, mercuric acetate, substituted thiohydantoin, antimicrobial activity.

Introduction:

Thiohydantoin is an imadazole derivative. Many of the physiologically compounds used in medicinal chemistry are imadazole derivatives, and thiohydantoin are important core moiety in the design and synthesis of active molecules as well as natural products Benzil (ȡ- diketone) condensed with thiourea1 and substituted thiourea2, 3 in alkaline ethanolic medium yielded thiohydantoin. these derivatives have not only been used in medicinal chemistry as anti-HSV, HDL-cholesterol modulators Thiohydantoin and its derivatives have been also used as fungicides 4, herbicides in agrochemical research 5-10 antidiabetic11, show anti HIV activity12, anticonvulsant13, antinociceptive activity14. Substituted thiohydantoin analogs as a novel class of antitumor agents15, antimicrobial activity16 and anti arrhythmic activity17 Recently synthesized thiohydantoin were tested for their activity against HIV-

118and showed potential selectivity against leukemia cell lines19 The preliminary bioassay showed that these compounds exhibit certain selectively herbicidal activities20

Material and Method:

Materials and methods The melting points were taken in open capillary tube, IR spectra were recorded on Perkin-Elmer spectrum RXI FTIR spectrophotometer21, 1H NMR spectra were recorded in CDCl3 on Bruker DRX-300 spectrometer operating at 300MHz. The purity of synthesized compounds was check by TLC. The structural elucidation of compound was done on the basis of chemical and spectral data. Preparation of 5-(2-hydroxy-3-nitro-5-chloro phenyl) 5- (ά-hydroxy-4-methoxy benzyl)-2-thiohydantoin (II a):- 2-(4"methoxy benzylidene)-5- chloro-7-nitro coumaran-3-one (I a) (0.01 mole) and thiourea (0.01 mole) were dissolved in 40 ml of ethanol. To this mixture 10 ml of 10% KOH was added drop wise with constant stirring, allowed to stand for 2 to 3 hours. The reaction mixture was refluxed for 3 hrs. Cooled and then diluted with ice cold water washed several time with 1% NaHCO3 solution and then with distilled water. It was then crystallized from ethanol to get 5-(2-hydroxy-3-nitro-5-chloro phenyl) 5- (ά-hydroxy-4-methoxy benzyl)-2-thiohydantoin (II a).

Result and Discussion:

The structure of compound (II a) has been supported by chemical data, it is deep buff color crystalline solid m. p. 126OC. it shows positive ferric chloride indicating non-involvement of phenolic –OH group, and spectral data. • An IR spectrum was recorded on Perkin-Elmer spectrum RXI FTIR spectrophotometer. 3852 cm-1(-N-H, stretching), 3853 cm-1 (-N-H, stretching), 3815-3801 cm-1 (-OH group stretching), 1805 cm-1 (Lactum cyclic C=S group stretching), 1511 cm-1 (-NO2 group symmetrical aromatic stretching), 1340 cm-1 (-NO2 group unsymmetrical aromatic stretching), 1251 cm-1 (-NH bond

stretching), 1060(-CHOH group stretching), 767cm-1(C-Cl group stretching). • 1H NMR in CDCl3 on Bruker DRX-300 spectrometer. δ=1.25(s, 1H,-CH), 3.9(s, 3H, Ar-OCH3 group), 6.3-6.4(d, 1H -OH), 6.8(m, 6H, Ar-H), 6.9-7.8δ(s, 1H, Ar-OH). These chemical and spectral data shows that compound (II a) is get 5-(2-hydroxy-3-nitro-5-chloro phenyl) 5- (ά-hydroxy-4-methoxy benzyl)-2-thiohydantoin.

Antimicrobial activities:

All the compounds have been screened for both antibacterial and antifungal activity using cup plate agar diffusion method21 by measuring the inhibition zone in mm. The compounds were taken at a concentration of 1 mg/mL using dimethyl sulphoxide as solvent

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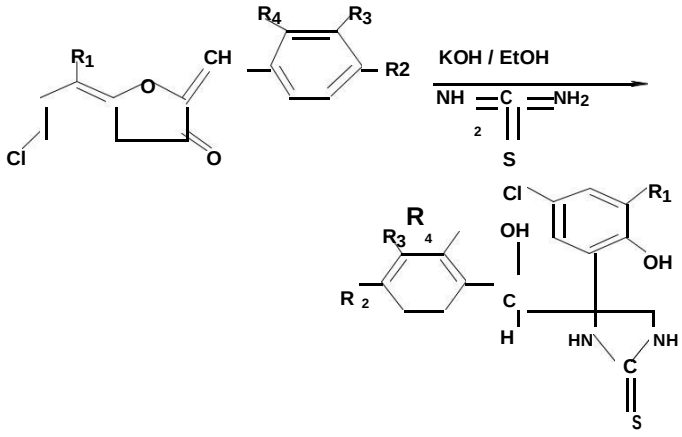
Table:-1 Synthesized compounds, M.P."s and yields.

S. No.	Compounds	R_1	R_2	R_3	R_4	M.P.(^{O}C)	Yield(%)
1	II a	NO_2	OCH_3	H	H	120	76
2	II b	NO_2	H	NO_2	H	126	78
3	II c	H	OCH_3	H	H	110	82
4	II d	Br	H	H	H	138	84
5	II e	Br	OCH_3	H	H	154	73
6	II f	Br	H	NO_2	H	132	76
7	II g	Cl	OCH_3	H	H	127	86
8	II h	Cl	H	NO_2	H	114	81



I (a) **II (a)**