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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ASSAY OF 1, 3, 5-TRIS [(2-HYDROXYNAPHTHALEN–1–YL)ALKYL]-2, 4, 6– HEXAHYDRO-[1, 3, 5] s-TRIAZINES

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Abstract— **β-Naphthol on treatment with amido/imidoalcohol in ethanol containing catalytic amount of conc. HCl afforded α-amido/imidoalkyl-β-naphthols (1), which on hydrolysis yielded 1-(aminoalkyl)-naphthalene-2-ols (2). Reaction of 2 with formaldehyde solution in ethanol furnished 1, 3, 5-tris [(2-hydroxynaphthalen-1-yl) alkyl]- 2, 4, 6-hexahydro[1, 3, 5] s-triazines (3) in moderate yields. Compound 3 have been evaluated for their antimicrobial activity in vitro involving four bacterial and five fungal strains.**

Index terms- **amido/alcohols, symmetrical triazines,**

I. INTRODUCTION

Triazines are associated with diverse biological properties viz; antiviral[1-3] diuretic[4, 5], and anti-cancer[6-7]. In continuation of our research efforts in the synthesis of bioactive heterocycles, we here in report the synthesis of 1, 3, 5- tris [(2-hydroxynaphthalen-1-yl) alkyl]-2, 4, 6-hexahydro[1, 3, 5] s-triazines **(3 a-d)** as target compound for studying their antimicrobial activity employing the standardized procedure as recommended by National Committee on clinical Laboratory Standards (NCCLS)[8, 9].

Synthesis of **1** is an example of C-α-amido/imidoalkylation reaction. This synthesis involved the interaction of β-naphthol and an amido alcohol (equimolar quantity) in ethanol solvent containing catalytic amount of conc. HCl **(2 ml).** Hydrolysis of **1** with NaOH solution followed by acidification afforded 1-(arylamido/imidoalkyl)-naphthalen-2-ols **(2)** as key intermediate, which on treatment with an excess equivalent of formaldehyde solution in ethanol furnished 1, 3, 5-tris [(2-hydroxynaphththalen-1-yl)alkyl]-2, 4, 6-dehydro-[1,3,5] triazines **(3).** The target compounds were characterized by their elemental and spectral (IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data).

II. PHARMACOLOGY

All the four compounds **(3 a-d)** were evaluated for their antibacterial activity against four bacteria viz; ***Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus,*** and *Klebsiella pneumonia*. Only two compounds viz; **3a** and **3b** showed promising antibacterial activity only against the bacterium ***Staphylococcus aureus*** since these two compounds had minimum inhibitory concentration values of **6.25** and **12.50,** respectively. These compounds were also screened for their antifungal activity against six fungi viz; ***Candida albicans, Cryptococcus neoformans, Sporothrix schenkii, Trichophyton mentagrophyte, Aspergillus flavus and Candida paraplosis.*** Only compound **3a** showed promising antifungal activity against ***Sporothrix schenkii*** and comparatively less significant antifungal activity against ***Candida albicans, Cryptococcus neoformans, and candida paraplosis.*** Other compounds **(3b, 3c and 3d)** displayed no measurable of antifungal activity.

III. EXPERIMENTAL

Melting points were determined in open glass capillary tube in Toshniwal melting point apparatus and the values reported herein are uncorrected. IR spectra were recorded on FT-IR Perkin Elmer (model) spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DRX-300 MHz spectrometer using TMS as an internal standard (the chemical shift values are expressed in ppm). FAB mass spectra were recorded on JEOLSX 102/DA - 6000 mass spectrometer. Purity of compound was checked by the silica gel G- plates and spots were visualized by exposure to iodine vapours.

α- (Arylamido/ imidoalkyl)-naphthols (1)

A mixture of β-naphthol **(0.1 mole)** and an appropriate aryl amido/imidoalcohol **(0.1)** mole in absolute ethanol **(100 ml)** containing conc. HCl **(2 ml)** was heated under reflux for two hours. Solvent was distilled off and the residual solid was washed with cold water. Dried at 100º C and recrystallized from diluted from diluted ethanol. The compounds of this category are presented in Table - 1.

1- (Aminoalkyl)–naphthalene-2-ols (2)

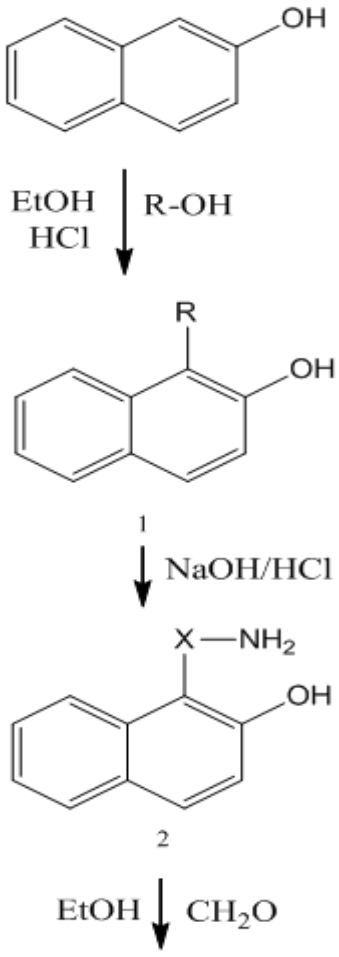
α-(Arylamido/imidoalkyl)-β-naphthol **(1) (0.05 Mole)** in sodium hydroxide solution **(10%) (50ml)** was heated under reflux for two hours. The resultant solution was allowed to cool at room temperature and acidified with dil. HCl. Precipitation occurred which was washed with 10% $NaHCO_3$ solution followed by cold water, at 100ºC, and recrystallized from dilute ethanol. The compounds thus synthesized are recorded in Table- 1.

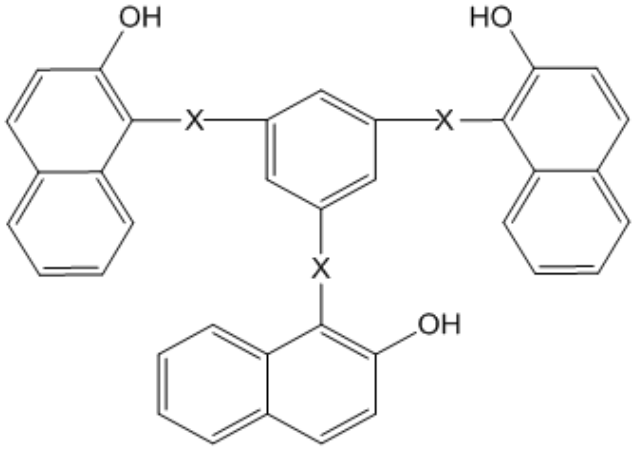
1, 3, 5-Tris[(hydroxynaphthalen-1-yl) alkyl] -2, 4, 6-hexahydro-[1, 3, 5] s-triazines (3)

1-(Aminoalkyl) naphthalen-2-ol **(2)** 1-(aminoalkyl) naphtalen-2-ol **(2) (0.01 mole)** was dissolved in ethanol **(50 ml)** by warming slowly. To this solution **40%** formaldehyde solution was added with stirring at room temperature. The resultant solution was further stirred for one hour and undisturbed. The solid thus separated out was filtered, washed with cold ethanol, and purified by extracting with boiling petroleum ether **(b. p. 80-100^0 C) (60ml).** After removal of the insoluble high polymer by hot filtration, the filtrate was cooled at room temperature and the product was filtered off. The symmetrical triazines thus synthesized are incorporated in Table - 1 along with characterization data.

IV. CONCLUSION

Triazines as antibacterial and antifungal agent have been less extensively investigated. However, such compounds have been extensively examined for their antiviral activity. Out of four triazines compounds screened for their antimicrobial activity, three are showing definite and measurable degree of activity. Such compounds are expected to confer improved therapeutic efforts if other pharmacophoric groups are introduce into the 2, 4 and 6 positions of the triazine nucleus.





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SCHEME

TABLE - 1

Characterization data of Compounds 1, 2, and 3

Compounds	R	X	m.p (%)	Yield (%)
1a	Phthalimidomethyl	–	174- 175	60
1b	Phthalimdoethyl	–	180-181	65
1c	Benzamdobenxyl	–	206-207	68
1d	Benzamidocinnamyl	–	216-217	65
2a	–	CH_2	161-163	55
2b	–	CH_2CH_2	110-111	50
2c	–	C_6H_5CH	159-160	55
2d	–	C_6H_5CH=CH-CH	163	60
3a	–	CH_2	152-153	48
3b	–	CH_2-CH_2	122	40
3c	–	C_6H_5CH	182	50
3d	–	C_6H_5CH=CH-CH	196-197	55

New compounds gave satisfactory elemental analysis.

IR (KBr) (in cm^{-1}): 3325 (ArOH), 3053 (C-H str. in aromatics), 1463(C-H def. Methylene), 1270 (C-O in phenol)

***^{1}H NMR(DMSO-D6) (in δ ppm):** 7.15-7.92 (m, 18H, Ar-H), 5.20(brs,3H,Ar-OH), 3.95(s, 6H, N-CH_2-N), 3.72(s, 6H,N-CH_2-C)

***^{13}C NMR ($CDCI_3$) (in δ ppm):** 70.2, 75.5, 112.5, 113.7, 117.5, 119.2, 121.4, 125.5, 131.5, 137.4, 141.2

***Mass (FAB):** M^+555, other important mass spectral peaks are m/e: 412, 398, 382, 226, 157, 140

Base peak appeared at m/e 157 for 2- hydroxy-naphthalene-1-yl methyl radical cation.

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