SYNTHESIS AND EVALUATION OF SOME 9-SUBSTITUTED ACRIDINES

P L N Ranganath
Department of pharmaceutical chemistry,
St.Johns college of Pharmaceutical sciences, Yerrakota, Yemmiganur-518360,
Andhra Pradesh, INDIA

Abstract
Acridines are the class of molecules which are known for their several biological properties like anti-bacterial, anti-malarial, anti-cancer and as well as dyes. Here are some 9-substituted acridines which are synthesized and screened for anti-bacterial and anti-fungal activities.

Keywords: Bernthsen Acridine Synthesis, 9-Substituted acridines, Antibacterial, Antifungal.

Corresponding Author:
P L N Ranganath
Department of pharmaceutical chemistry,
St.Johns college of Pharmaceutical sciences,
Yerrakota, Yemmiganur-518360,
Andhra Pradesh, INDIA
E-mail: prathapagiri.pln@gmail.com
Phone: +91- 8985213402

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INTRODUCTION

Acridines are the class of molecules which gained much synthetic interest due to their usage as dyestuffs and the acridine derivatives possessing profound biological properties like anti-bacterial properties antifungal, anticancer, anti malarial and many other properties [1,2]. These are well-known nitrogen heterocyclic compounds having wide range of biological activities like antibacterial, anticancer, antitumor, anti-viral and so on. Here I prepared a series of compounds of 9-substituted acridines, which were synthesized by following Bernthesen Acridine Synthesis reaction [3] and are screened for antibacterial and antifungal activities [4-6].

![Bernthesen Acridine Synthesis](Fig.1)

MATERIALS AND METHOD

All the chemicals and solvents used in this study were of analytical grade (S.D. FINE Chem. Limited, Mumbai). All the solvents were freshly distilled standard drying agents. Spectral data $^1$H NMR of all compounds were recorded on Avance spectrometer 300 MHz. IR spectra were obtained using Perkin Elmer model 237B spectrometer. Melting points of the synthesized compounds were determined by open capillary method and were uncorrected.

GENERAL PROCEDURE OF SYNTHESIS OF SUBSTITUTED ACRIDINES (1-5) [3]

9-Substituted acridines were prepared by stirring a mixture of diphenylamine (40 mmol) in ethanol (20 mL), carboxylic acid (R-COOH) (20 mmol) where R- Carbamic acid (1), Acetic acid (2), Thioglycolic acid (3), Nitrobenzoic acid (4), Benzoic acid (5). To each of the above stirred amine and carboxylic acid mixture in ethanol, Phosphoric acid (10 mmol) was added and stirred for 3h at 150$^0$C. The reaction was monitored with the TLC. After the completion of reaction, the reaction mixture was extracted with ethylacetate (3 x 30 mL). The latter organic phases were

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combined and dried (Na₂SO₄). After concentration under reduced pressure, the residue was purified by column chromatography on silica gel by using the eluent ethylacetocetate and cyclohexane (2:8).

**ANTIBACTERIAL & ANTI FUNGAL STUDIES**

All the derivatives were screened for antimicrobial and antifungal activity using cup-plate method. In this method the microorganisms B.Subtilis (Gram positive), E.Coli (Gram negative), C.albicans and A.niger (Fungi) were used. Above said microbes are subcultured in an Nutrient agar medium. Minimum Inhibitory Concentration (MIC) of the all derivatives was determined. The MIC is the lowest concentration of tested compounds that completely inhibited the growth of the test organisms after 24 and 48 h of incubation at 37°C and 27°C for bacteria and fungi, respectively by using the control DMSO and standard drugs Ampicillin (100μg/ml) and Ketocanazole (100μg/ml) for antibacterial and antifungal studies.

<table>
<thead>
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<th>Table 1: Zone of inhibition (diameter in mm)</th>
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<tr>
<td>Compound</td>
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**RESULTS AND DISCUSSION**

**Acridin-9-amine (1)**

\(^1^H\) NMR (300 MHz, CDCl₃): \(\delta = 7.45\) (m, 2H), 7.68 (m, 2H), 7.59 (d, 2H), 8.12 (d, 2H), 5.24 (s, 2H). IR (KBr): \(\bar{\nu} 3036, 2948, 2875, 1386, 1378, 1115, 995, 635\) cm.\(^{-1}\); \(m/z\) 195 (M+H)\(^+\)

**9-methylacridine (2)**

\(^1^H\) NMR (300 MHz, CDCl₃): \(\delta = 7.45\) (m, 2H), 7.68 (m, 2H), 7.59 (d, 2H), 8.12 (d, 2H), 3 (s, 3H). IR (KBr): \(\bar{\nu} 3367, 3298, 3097, 1786, 1258\) cm.\(^{-1}\); \(m/z\) 194 (M+H)\(^+\)

**9-propylacridine (3)**

\(^1^H\) NMR (300 MHz, CDCl₃): \(\delta = 7.45\) (m, 2H), 7.68 (m, 2H), 7.59 (d, 2H), 2.4 (m, 2H), 1 (m, 2H), 1 (m, 3H). IR (KBr): \(\bar{\nu} 3298, 3197, 3036, 1386\) cm.\(^{-1}\); \(m/z\) 223 (M+2H)\(^+\)

**9-(4-nitrophenyl) acridine (4)**

\(^1^H\) NMR (300 MHz, CDCl₃): \(\delta = 7.45\) (m, 2H), 7.68 (m, 4H), 7.59 (d, 2H), 8.12 (m, 4H), IR (KBr): \(\bar{\nu} 3298, 3197, 3036, 1386, 1310\) cm.\(^{-1}\); \(m/z\) 302 (M+2H)\(^+\)

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9-phenylacridine (5)

$^1$H NMR (300 MHZ, CDCl3): $\delta = 7.52$ (m, 6H), 7.8 (d, 2H), 8 (m, 4H),. IR (KBr): $\tilde{v}$ 3298, 3197, 3036, 2968, 1386 cm.$^{-1}$; m/z 256 (M+H)$^+$

All the synthesized 9-substituted acridines (1-5) shown antibacterial and antifungal activities as shown in the in the table 1 against the microbes (E.coli, B.subtilis) strains (A.niger, C.albicans).

CONCLUSION

In conclusion, we successfully synthesized the substituted acridines by using Berthnesen reaction and are screened for antibacterial and antifungal activities.

ACKNOWLEDGEMENT

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REFERENCE

3. A. Bernthsen, Formation of 5-substituted acridines by heating diarylamines in organic acids or anhydrides, usually in the presence of zinc chloride Ann. 192, 1 (1878); 224, 1 (1884).