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Synthesis Of Acridine And Its Derivative With Reference To Their Antibacterial Activity

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ABSTRACT

A new efficient procedure for the synthesis of 9(2-chlorophenyl aridine) under microwave irradiation and derivatives were characterized by different spectral technique IR and NMR spectroscopy. Reactions proceed with very good to excellent yield at room temperature. Further were screened for their in vitro antibacterial activities against pathogenic bacteria such as Salmonella typhi, Proteus vulgari, Klebsiella pneumonia, E. Escherichia, Shigella Flexner (gram –ve) and Staphylococcus area (gram +ve) bacteria by using agar-agar well diffusion meth- od. The results were evaluated after 24 hour of incubation. Chloro-substituted compounds showed antibacterial activity values in the low microbial range.

Keywords: Acridine, spectral analysis, antibacterial efficacy.

INTRODUCTION

Acridine is a heterocyclic nucleus. It plays an important role in various medicines. A number of therapeutic agents are based on acridine nucleus such as quinacrine (antimalarial), amsacridine and nitracine (anticancer) and terrine (1). It is characterized by its irritating action on skin and by the blue fluorescence showed by solution of its salts (2). The structure activity relationship of acridine antibacterial was established by an Australian Chemist Adrien Albert. The finding of his study indicated that cationic ionization and planar molecular surface are = 38 A^O Is Necessary for antibacterial activity. However the contemporary antibacterial therapy In literature, It has been found that acridine derivatives possess widely differing activities such as ant inflammatory and anticancer (3), anthelmintic (4), insecticidal, rodenticide (5) fungicidal (6) antitumor activities (7) Acridine are a well-known group of compound (8) biological properties (9). There are several approach- es to their synthesis. Brethren reaction is one classical method. It is mainly the heating of diphenylamine in presence of zinc chloride and a carboxylic acid, temperature of reaction is 200-210^0 C and reaction are low. In our group we are interested in the application of microwave heating to organic synthesis (10) cyto- toxic (11) it is an antineoplastic agent (12).

MATERIAL AND METHODS

EXPERIMENTAL

Synthesis of 9- Phenylacridine: A mixture of Diphenylamine (1mmol), Benzoic acid (1 m mole), 5ml Ethanol, (0.5 m mole) $BaCl_2$ as a catalyst was placed in 100 ml conical flask and mixed toughly. A mixture was irradiated microwave oven (MW domestic type oven 800W SANYO) at 10 % intensity for 12 min. (six pulses each of 2 min.). After completion of reaction (by TLC), the mixture was poured into ice-cold water. The separated solid was filtered, washed with excess of cold water and dried at room temperature for 20 min. After completion of reaction, the resulting mixture poured into crushed ice crude product was dried and further purified by crystallization from ethanol to afford pure 9- Phenylacridine . The melting point of product was recorded 186^0C.

Synthesis of 2(acridine-9-yl) benzamine: A mixture of Diphenylamine (1mmol), anthracitic acid (1 m mole), 5ml Ethanol, (0.5 mmol) $BaCl_2$ as a catalyst was placed in 100 ml conical flask and mixed toughly. A mixture was irradiated microwave oven (MW domestic type oven 800W SANYO) at 10 % intensity for 12 min. (six pulses each of 2 min.). After completion of reaction (by TLC), the mixture was poured into ice-cold water. The separated solid was filtered, washed with excess of cold water and dried at room temperature for 20 min. After completion of reaction, the resulting mixture poured into crushed ice crude product was dried and further purified by crystallization from ethanol to afford pure 2(acridine-9-yl) benzamine . The melting point of product was recorded-276^0C

Synthesis of 9 (2-Chlorophenyl) acridine: A mixture of Diphenylamine (1mmol), O-chlorobenzoic acid (1 mmol), 5ml Ethanol, (0.5 mmol) $BaCl_2$ as a catalyst was placed in 100 ml conical flask and mixed toughly. A mixture was irradiated microwave oven (MW domestic type oven 800W SANYO) at 10 % intensity for 12 min. (six pulses each of 2 min.). after completion of reaction (by TLC), the mixture was poured into ice-cold water. The separated solid was filtered, washed with excess of cold water and dried at room temperature for 15 min. After completion of reaction, the resulting mixture poured into crushed ice crude product was dried and further purified by crystallization from ethanol to afford pure 9 (2- Chloro-phenyl) acridine . The melting point of product was recorded-226^0C.

Synthesis of 9- Methyl-acridine: A mixture of Diphenylamine (1mmol), Acetic acid (1 mmol), 5ml Ethanol, (0.5 mmol) $BaCl_2$ as a catalyst was placed in 100 ml conical flask and mixed toughly. A mixture was irradiated microwave oven (MW domestic type oven 800W SANYO) at 10 % intensity for 12 min. (six pulses each of 2 min.). After completion of reaction (by TLC), the mixture was poured into ice-cold water. The separated solid was filtered, washed with excess of cold water and dried at room temperature for 15 min. After completion of reaction, the resulting mixture poured into crushed ice crude product was dried and further purified by crystallization from ethanol to afford pure 9- Methyl acridine . The melting point of product was recorded-121^0C.

RESULT AND DISCUSSION

Synthesis of acridine derivatives: The result obtained in the present research work showed that this new synthetic pathway would give rise to design of better molecule having good yields of acridine and its derivatives.

SPECTRAL ANALYSIS

1H NMR spectral analysis:
δ 7.72 (d 2H, J= 9.3Hz, Ar-H), δ 7.64 (d, J= 9.4 Hz ,Ar-H), δ 7.41-7.48 (m, 4H Ar-H).
IR-The general spectral characterization show absorption bond correspond the 1660 cm-1for v(C=N) stretching of acridine moiety. Weak absorption band occur at 830 cm^{-1} (C-Cl) the most prominent bond due to (–C=N-C) stretch occur at range 3383.14cm-1. It is also observe that strong band at 1680 cm-1 due to v (c=c) stretching

EVALUATION OF ANTIBACTERIAL PROPERTIES

Synthesized 9(2-chlorophenyl acridine) and its derivatives were screened for their antibacterial activities against pathogenic bacteria such as Salmonella typhi, Proteus vulgaris, Staphylococcus areas, Klebsiella After incubation for 24 hour, samples were analyzed for zone of inhabitation. It was observed that 9(2- chloro-phenyl aridine) shows specific antibacterial activity against gram negative bacteria (Salmonella typhi, Proteus vulgaris, Klebsiella pneumonia, Escherichia, Shigella Flexner and gram positive (Staphylococcus aureus). The compound (Staphylococcus aureus) gram positive shows remarkable activities against bacterial pathogen. It was observed that the higher activity of above synthesised compound is due to presence of heterocyclic ring structure containing Nitrogen atom. The heterocyclic ring containing these atoms increases the efficacy of compound. Showing the activity of all the bacteria are gram negative, found in all synthesizes compound less high activity against Salmonella typhi (fig 1). Molecules containing the 9(2-chlorophenyl aridine) heterocyclic ring com- pound show wide range of antibacterial activities. Compound so obtained were further investigated for their antibacterial activity which show some significant results against Gram- negative (Salmonella typhi, Proteus vulgaris, Klebsiella pneumonia, E-coli, Shigella Flexner) bacteria proposed compared with Gram-positive (Staphylococcus aurous) bacterial.

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