A LITERATURE SURVEY ON THE SYNTHESIS OF DIFFERENT AMIDOALKYLATED PRODUCTS FOR THEIR STUDIES AS DIFFERENT BIOACTIVE COMPOUNDS

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ABSTRACT

The acquisition of new chemical agents with chemotherapeutic value in the fight of biological disorders is of high importance for the researchers in modern medicine. The screening programme aims at finding sources at biologically active chemical agents for the development of the drugs and at discovering the lead molecules that can be modified through chemical means into useful drugs. This effort is multidisciplinary in nature and involves the active participation of chemists, pharmacologists, toxicologists, clinicians and others. The chemists produce several thousand new compounds involving various chemical methods every year as potential drug. The pharmacologist has numerous ways of screening these compounds in various animal species. Due to limited amount of material generally available initially and high cost of biological testing, it is very difficult in any single laboratory to examine all permuations of these materials. The pharmacologist is, therefore, called upon to make use of his experience and inventiveness to limit the tests to those likely to be most rewarding in existing situation. This necessitates the development of a screening programme for initial detection and some quantifications as well as classification of biological activity. Even though all screening programmes have these amis, no two screening programmes can be identical. The informations obtained by the initial or primary information is predominantly descriptive and qualitative leaving the analytical 'in depth' evaluation to a later stage called the 'followup' or 'secondary screening'.

***Keywords**: Amidoalkylation, polyalkylation, rearrangement*

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INTRODUCTION

a-Amidoalkylation reaction particularly, amidomethylation and amidoethylation is perhaps the most convenient, appropriate and useful procedure for the synthesis of a wide variety of compounds of biological and theoratical interest leading to the. Formation of new carbon-carbon bond. In certain instances, viz; with 8-hydroxyquinoline, amidoalkylation reaction proceeds to give cyclic compounds of biological significance. This is an example of intramolecular a-amidoalkylation reaction under thermal reaction conditions. Other methods of alkylation viz; Michael condensation, Witting reaction, Mannich reaction, Friedal-Craft's alkylation reactions, cyanoethylation etc. require comparatively more drastic reaction conditions as compared to a-amidoalkylation reaction where reaction conditions are very simple and less drastic. In addition, polyalkylation or rearrangement leading to the formation of other compounds than expected is not observed with a-amidoalkylation reaction. The reaction can be accomplished and completed in shorter period of time with excellent yields. There are a variety of choices in order to carry out this reaction in the laboratory and this reaction can be attempted effectively with mineral acid catalysts such as conc. sulphuric acid alone, a mixture of conc. H_2SO_4 and glacial acetic acid, methane sulphonic acid, phosphoric acid, hydrochloric acid in ethanol or methonol etc. Lewis acid catalysts which have been commonly employed include anhydrous aluminium chloride, zinc chloride, stannic chloride and boron trifluoride as well as iron chloride in certain cases. Thermal amidoalkyloation reactions have been attempted while synthesizing the compounds of biological significance specifically in the preparation of the derivatives of secondary amines like that of benzimidazole, phenothiazine, indole etc. a-Amidoalkylation reaction unlike the corresponding a-aminoalkylation reactions probably encompasses a considerable portion of mechanistic spectrum of heterolytic organic chemistry. Detailed studies are almost lacking. Nevertheless, some general outlines of the mechanistic possibilities can be drawn. a-Amidoalkylation reaction bears a superficial relationship to the well known Mannich reaction. However, the latter is usually restricted to the preparation of tertiary benzylamines whereas amidoalkylation through hydrolysis of initial product provides a route to primary benzylamines. Furthermore, the scope of Mannich reaction in aromatic series is generally restricted to phenol or to equally nucleophilic ring systems.

In contrast, some of the reagents available for amidoalkyation are even more electrophilic than the usual acylation reagents of the Friedal-Craft's reaction. Consequently, the scope of some of the amidoalkylations can be extended to aromatic systems usually considered rather inert to substitution Compounds sufficiently nucleophilic to undergo attack by the amdoalkylating agent include aromatic compounds, olefins, alkynes, ketenes, carbenoid compounds and carbanionoid compounds derived from active methylenes, Grignard reagents and other organo metallics.

A few amidoalkylations have been affected using formaldehyde with amides or acetonitriles to produce the Nhydroxy methyl amide in situ. An important recent development in amidoalkylation has been the direct substituttion of aromatic compounds by N-a-hydroxy

alkylamides, derived from glyoxyllic acid. The high order of reactivity of N-chloroalkylamides often prevents their isolation and purification with aromatic compounds. Therefore, they are frequently made from N-a-hydroxylakyl precursors and treated further substrate and catalyst without isolation. Also use of precursors can lead to more structural diversity perhaps the most significant application of amidoalkylation reaction has been in the synthesis of polymers. The normal addition of alcohols or their derivatives to nitrites under acidic conditions leads to the formation of iminoester salt or esters. Certain secondary and tertiary amines or related olefins, however, add abnormally to give N-substituted amides. It has been shown that N-methylol amides reacted with nitriles in a similar abnormal manner to give amides of methylenediamines. A related reaction of two moles of an aromatic nitriles with one of formaldehyde to give methylene bis amides in the presence of excess of mineral acids has been known for many years.

A preliminary extension of this reaction to aliphatic mononitriles indicated that the reaction was rapid and essentially quantitative. Studies were then initiated in an effort to produce polyamides of higher molecular weight from a number of aliphatic dinitrite from three to ten carbon atoms. The formaldehyde azelanonitrile reaction was selected for detailed study since the thermal (m.p. 245-250°C) and solubility (soluble in only in phenol and formic acid) characteristics of the resultant polymethylene azelamide approximated those of commercial polyhexamethylene adipamide.

$$n - NC(CH_2)_7CN + n.CH_20 \xrightarrow[H20]{} \xrightarrow{H2SO4} [NHCO(CH_2)7CONHCH_2]n$$

As expected methylenepolyamides having a lower carbon to nitrogen ratio, prepared from lower straight chain aliphatic dinitrile, melted at higher temperature and were less soluble. After a systematic study a reaction variables it was possible to prepare polymethylneazelamide having specific viscosities of 0.9 to 1.2 for a 1% solution in ethanol. These values are comparable to those found for samples of commercial flake Nylon which has been shown to have molecular weight of approximately ten thousand.

A large majority of aromatic amidoalkylations reported upto date have been conducted either in conc. sulphuric acid, according to Tscherniac's original specifications or in the ethanolic hydrogen chloride medium used by Einhorn for nucliophilic aromatic systems. Despite the long history, remarkably few attempts to vary the conditions of the Tscherniac Einhorn reaction have been reported. Even fewer qualify as reasonably systematic studies of reaction conditions.

The acquisition of new chemical agents with chemotherapeutic value in the fight of biological disorders is of high importance for the researchers in modern medicine. The screening programme aims at finding sources at biologically active chemical agents for the development of the drugs and at discovering the lead molecules that can be modified through chemical means into useful drugs. This effort is multidisciplinary in nature and involves the active participation of chemists, pharmacologists, toxicologists, clinicians and others. The chemists produce several

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For the development and designing of new compounds of biological significance there are several stages viz; preparation of new compounds by synthesis, its proper characterization and identifications by chemical and spectral methods, its acute toxicity test, its radiochemical and biochemical studies, its evaluations for a particular symptom on experimental animals and finally its chemical trial. To produce its characteristic effects a drug must be present in appropriate concentrations at its site of action. The concentration attained also depends upon the rate of its absorption, distribution, binding or localizations in tissues, biotransformation and excretion. It is of practical importance to know the manner in which the drugs are absorbed. Often there is a choice of the route by which therapeutic agent may be given and a knowledge of advantage and disadvantages of different route of administration is then of primary significance. Modern chemotherapy has markedly improved the drug delivery system. Attempts have been made to devise the methods in which the drug hits the target site by slow biodegradability and a major part is available for exerting biological response. Since a wide variety of new compounds can be synthesized involving amidoalkylation reaction, viz; aliphatic, aromatic, heterocyclic, semiaromatic etc it is thought that introduction of amidoalkyl groups in such class of compounds might confer better therapeutic results because of several reasons viz; increase in the polarity of compounds, increase in the hydrrophilic character of compounds etc. In addition, an investigation in this field underoubtedly provides an opportunity to prepare more powerful electrophilic reagents (amido alcohols), so that they may react with weaker nucleophilic reagents like cyclohexanone etc. under the identical reaction conditions.

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