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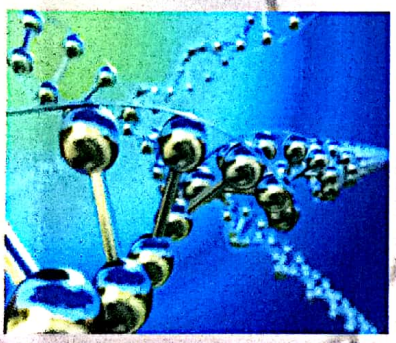

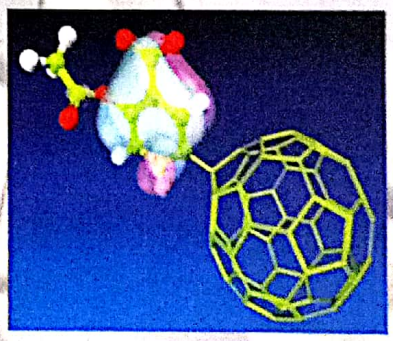

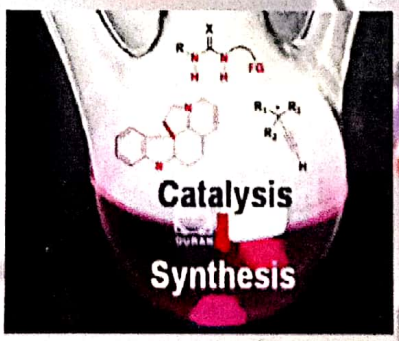

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Department of Chemistry And Analytical Chemistry

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A Novel Synthesis of 4-methyl-2H-1,2,4-benzothiadiazine-3(4H)-one 1,1-dioxide

Anil B. Chidrawar

Department of Chemistry, Degloor College, Degloor-431717, S.R.T.M.U. Nanded, Maharashtra, India.

Email : anilchidrawar74@gmail.com

Abstract : An efficient method have been used for the synthesis of 4-methyl-2*H*-1,2,4-benzothiadiazine-3(4*H*)-one 1,1-dioxide (3) obtained by the reaction of N-methyl aniline (1) with chlorosulfonyl isocyanate (2) in nitromethane followed by cyclization with aluminium chloride. The structures for the synthesized compounds are assigned on the basis of IR, ^{1}HNMR and Mass spectral studies.

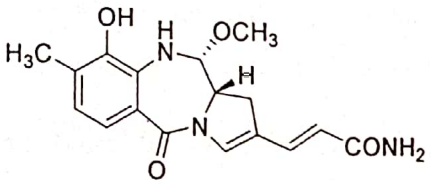
Keywords : N-methyl aniline, chlorosulfonyl isocyanate, nitromethane and aluminium chloride.

Introduction : Sulfonamides have been clinically used for many years and found to possess a large number of biological activities, including antibacterial, anticancer. Cancer is a disease caused by the malfunctioning of normal cells. It is one of the most feared diseases due to a general perception that it is an indiscriminate and incurable affliction that insidiously attacks people of all cultures and ages. Chemotherapy of the use of chemical agents to destroy the cancer cells is a mainstay in the treatment of malignancies. Though, the classical treatment of cancer, typically involves surgical removal of tumours or destruction by localized radiotherapy, chemotherapy is of utmost importance in order to ensure that all the malignant cells, including any meta-stats are destroyed.

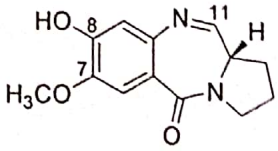
Cancer chemotherapy may also improve both patient survival and well being to variable extent. Thus, there is no doubt an essential role for chemotherapeutic drugs in contemporary clinical oncology. The development of the area of anticancer drug discovery basically reflects an evolution from highly empirical approaches, based on serendipitous findings and testing of randomly selected compounds, to the current, more focused testing of natural products, rationally synthesized agents, and biological products against panels of well-characterized tumour cell lines or molecular targets. The major categories of chemotherapeutic agents are naturally occurring antitumour antibiotics, DNA interactive

agents, enzyme inhibitors such as cyclin-dependent kinase, carbonic anhydrase, tubulin polymerisation, topoisomerase I and II etc. which play key role in cell division.

The pyrrolo[2,1-*c*][1,4]benzodiazepines (PBDs) are well known class of antitumour antibiotics with sequence selective DNA binding ability that are derived from various *Streptomyces* species. The first pyrrolo[2,1-*c*][1,4]benzodiazepine antitumour antibiotic anthramycin has been described by Leimgruber co-workers in 1963, and since then a number of compounds have been developed on PBD ring system leading to DNA binding ligands. Their mode of interaction with DNA has been extensively studied and it is considered unique as they bind within the minor groove of DNA. These compounds exert their biological activity by covalently binding to the C2-amino group of guanine residue in the minor groove of DNA through the imine or imine equivalent functionality at N10-C11 of the PBD moiety.



Anthramycin



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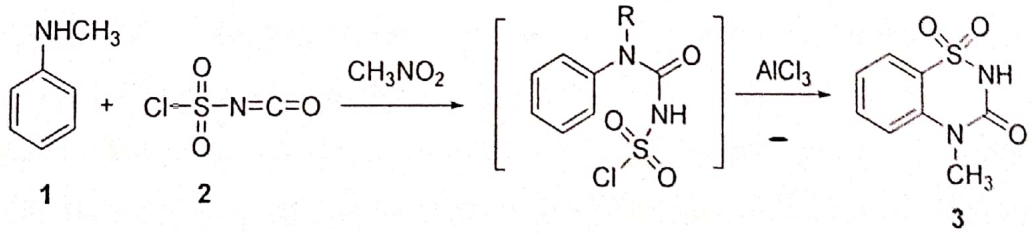
Material and methods :

Design, Synthesis, DNA binding affinity and cytotoxicity of 4-methyl-2*H*-1,2,4-benzothiadiazine-3(4*H*)-one 1,1-dioxide

Benzothiadiazines derivatives have attracted intense interest in recent years because of their diverse pharmacological properties including anticancer activity. The objective of the present work is the synthesis of new benzothiadiazine and study their DNA binding affinity as well as *in vitro* anticancer activity. N-methyl aniline (**1**) on treatment with chlorosulfonyl isocyanate (**2**) in nitromethane followed by cyclization with aluminium chloride gives 4-methyl-2*H*-1,2,4-benzothiadiazine-3(4*H*)-one 1,1-dioxide (**3**).



1 2 3

Discussion :

Antibacterial research over the past 50 years has been focused on meeting medical needs caused by infectious, life-threatening pathogens. In spite of the introduction of a variety of

antibacterial agents in multiple unrelated drug classes, resistance continues to emerge. Sulfanilamide, and the other sulfa drugs, are analogs of p-aminobenzoic acid (PABA); they compete with PABA and, block the synthesis of folic acid. The sulfonamides class includes several antibiotics, including sulfamethoxazole, sulfasalazine, and sulfacetamide, among others. Sulfonamides were effective inhibitors of the biosynthesis of folic acid compounds by cell-free extracts of Escherichia coli.

Conclusion :

Benzothiadiazine ring system has been considered as cyclic sulfonamides and these derivatives have shown strong activity against several cancer cell line. Furthermore, fused 1,2,4-benzothiadiazine-1,1-dioxides as potential α_1-adrenoreceptor antagonists as well as anticancer agents and styryl benzothiadiazine have exhibited antitumour activity by inhibiting tubulin polymerization.

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