E2-16: Synthesis of potent Bio-active 1,3,5-trioxygenated-9-acridone Alkaloids

H M T B Herath, H V K Diyabalanage
(*Synthetic Organic Chemistry, Institute of Fundamental Studies, Kandy*)

Acridone alkaloids constitute a small group of natural products found mainly in the Rutaceae family of higher plants. This class of compounds has generated considerable interest in view of the reported broad and higher anti tumour activity of acronycine and the versatile biological activity of other acridones. Since most of the biologically active acridone alkaloids including acronycine have 1,3-dioxygenated system, our interest was focused on the synthesis of different types of naturally occurring and new acridone alkaloids with oxygenated functions at 1 and 3 positions with the view to determine the methodology of synthesis and also to provide these compounds for pharmacological studies.

Treatment of 2-amino-3-hydroxybenzoic acid with phloroglucinol gave 1,3,5-trihydroxy-9-acridone (A). Methylation of A with MeI in the presence of KOH in DMSO at 5 - 10°C followed by preparative TLC gave 1,3,5-trimethoxy-10-methyl-9-acridone (**1**) which has been reported as natural product form *Teclea boiviniana* and 1,3,5-trimethoxy-4, 10-dimethyl-9-acridone (**2**). Demethylation of 1 by refluxing with 48% HBr yielded, 1,3,5-trihydroxy-10-methyl-9-acridone (**3**) as a single product. Compound **3** has been to be reported as an acridone moiety of the acridone-coumarian dimer (Acrimarin-G), isolated from *Citrus funadoko* and the root of Yahala (hybrid of several *Citrus* species). A mixture of 2-amino-3-methoxybenzoic acid, phloroglucinol and p-toluenesulphonic acid in hexanol at reflux temperature for 12h gave 1,3-dihydroxy-5-methoxy-9-acridone (**4**) as a major product.

The structural elucidation of the above compounds were done on the basis of ^{1}H and ^{13}C NMR spectral data and the confirmations were done by comparison with the previously reported values whenever possible and also by using Heteronuclear Multiple Quantum Coherence (HMQC) and Heteronuclear Multiple-Bond Correlation (HMBC) spectral data wherever necessary.