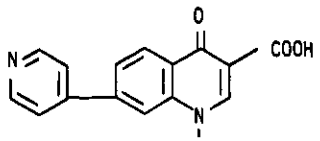
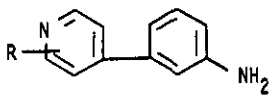
Pyridine Chemistry in the Preparation of Two Medicinal Agents: Rosoxacin and Amrinone

George Y. Lesher,
Sterling-Winthrop Research Institute
Rensselaer, NY 12144

In this talk I will cover the chemistry involved in the development of the antibacterial agent rosoxacin. The emphasis here will be on the variety of ways that were employed to prepare the anilino-pyridine intermediates.

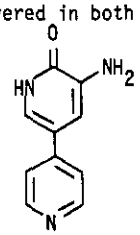


rosoxacin



anilino-pyridine

This will be followed by a description of the chemistry used in the preparation of amrinone, a new cardiotonic agent, and a variety of related compounds. The chemistry covered in both of these areas will generally be



amrinone

that used to build pyridine rings and manipulate attached functionality. A minimum of biology will be presented to justify why we were doing what we were doing.

Halogenated Pyridines: Their Synthesis and Applications to Several Areas of Crop Protection

Howard Johnston,
Dow Chemical U.S.A.
Agricultural Products Research
P. O. Box 9002
Walnut Creek, CA 94598

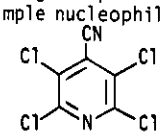
This talk will be concerned with the synthesis and chemistry of a number of biologically active pyridine derivatives. The emphasis will be mainly on halogenated pyridine carboxylic acids, pyridinols and their precursors.

Polyactivated Polychlorinated Pyridines

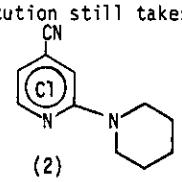
Basil J. Wakefield,
Department of Chemistry and Applied Chemistry,
University of Salford,
Salford. M5 4WT U.K.

The chemistry of pentahalogenopyridines is well explored, and is, dominated by reactions involving nucleophilic substitution in the α- and γ-positions. Even intramolecular substitution at a β-position of pentachloropyridine has been observed in only a few cases. We have studied the possibility that a strongly electron-withdrawing group at the γ- (or an α-) position would activate the β-positions sufficiently

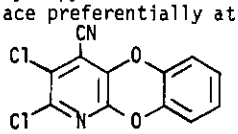
for nucleophiles to attack these preferentially. As nucleophiles react with tetrachloro-4-nitropyridine or tetrachloro-4-alkylsulphonyl-pyridines by displacement of the 4-substitutent, our studies have been directed mainly to tetrachloro-4-cyanopyridine (1), which is prepared by high-temperature gas-phase chlorination of 4-cyanopyridine. With simple nucleophiles, substitution still takes place preferentially at



(1)



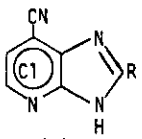
(2)



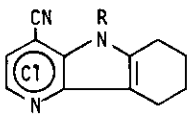
(3)

an α-position to give compounds such as the piperidino-compound (2). With bidentate nucleophiles, however, attack at both 2- and 3-positions gives new heterocycles; catechol, for example, gave the benzodioxino-pyridine (3).

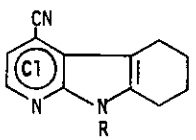
The principles established by the work described above have been extended to the synthesis of compounds of possible biological interest. Reactions of tetrachlorocyanopyridines with amidines have so far failed to give imidazolopyridines such as (4), but reactions with enamines



(4)



(5)



(6)

gave tetrahydrocarbolines (5) and (6). The reaction leading to the tetrahydrocarbolines has been studied in some detail, and the results will be discussed.

Pyridine with Polyfunctionalized Appendages

George R. Newkome,
Department of Chemistry,
Louisiana State University,
Baton Rouge, LA 70803.

Over the past few years, we have entered into an area of study in which metal ions as well as neutral organics are inclusioned within a neutral host. In order to better understand the fine-points and be able to predict the optimal guest-host relationship, our recent research activities have dealt with: synthetic aspects, molecular ion and molecule inclusion, site geometries, organometallic spin-offs, catalytic activities, polymer binding, and computer design. After a brief historical introduction of my entry into pyridine chemistry, this presentation will highlight our recent synthetic and structural adventures in pyridine chemistry.