ABSTRACT

Thesis: Chemistry of Quinoline-2-Carbaldehyde Derivatives with Malononitrile and Formation of Indolizines

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The quinoline-5,8-diones are an important class of compounds with a wide spectrum of biological activites such as antibacterial, antiasthmatic, antifungal, antitumour and antiparasitic agents. Over the past three decades many variously substituted derivatives of quinoline-5,8-diones have been synthesized and reported. The majority of them dealt with the chemistry of C-6 and/or C-7 substituted quinolinediones and were related to Lavendamycin.

Our lab has developed several procedures for the condensation (Knoevenagel) and reduction of aldehydes and ketones with malononitrile. When this reductive alkylation procedure was attempted with quinoline-2-carboxaldehyde, a crude product was observed by NMR spectroscopy. This product rearranged upon attempted purification via recrystallization or column chromatography. The nucleophilic attack of the quinoline N

on the C of the nitrile followed by a proton transfer and a tautomerization resulted in the creation of indolizine.

We will study the reductive alkylation of a series of quinoline-5,8-diones with carboxaldehydes at the C-2 position with malononitrile. This reaction is carried out in 95% ethanol with no catalysts present. This reaction mixture is then diluted with additional 95% ethanol and then cooled in an ice/water bath before the addition of sodium borohydride ($NaBH_4$) to afford the desired monosubstituted malononitrile.

We have also carried out the reactions with a range of other substituted quinoline compounds. In these cases the indolizines were not observed. It is assumed that the indolizine product does not form due to the presence of substituents on the C-8 position. Additional studies will focus on unsubstituted C-8 quinoline rings to prepare other novel indolizines. Otherwise, various reactions are performed to force the formation of indolizine.