SYNTHESIS OF QUINAZOLINES AND 1,4-BENZODIAZEPINES

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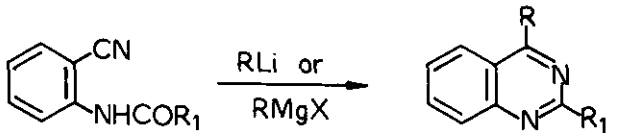
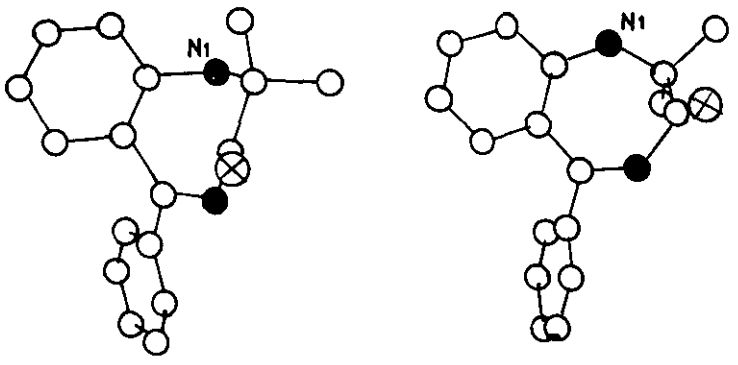
Addition of RMgX or RLi to N-acylated anthranilonitriles (1) has been found to be a general, fast and convenient route to quinazolines of the general strucuture 2.



1 2

The reaction is considered to involve formation of an anion of an imine in the initial step. Consequently one might expect the formation of e.g. 1,4-benzodiazepines with 1, R_1= CXR_2R_3 (where X is a suitable substituent such as Cl or Br) as reactant. The product pattern was found to be highly dependent on the substituents. Thus, whereas 1, R_1 = CH_2Cl with C_6H_5MgX gave 2 (R = C_6H_5, R_1 = CH_2Cl) 1, R_1 = $CHClC_6H_5$, with the same reagent gave the known compound 3,5-diphenyl-1,4-benzodiazepine-2-one. The case C_6H_5MgX + 1, R_1 = $CBr(CH_3)_2$, was found to be of special interest as it seems to involve initial formation of an aziridinone followed by intramolecular ring-opening to yield 3, which was found to occur in two forms. Conformer 3a (believed to be closer to the intermediate aziridinone) was unstable and could readily be converted into 3b.



3a 3b