ABSTRACT.

The reaction of hydroxyacetylenic nitriles with 2-aminoethanethiol gives 3-(2-aminoethylthio)-4-hydroxyalkyl-2-enenitriles. These do not cyclise directly to a furan but first isomerise to the corresponding N-adducts which then cyclise to give 5-amino-3-(2-thioethylamino)-2,2-dialkyl-2,3-dihydrofurans in > 90% yield.

After protecting the hydroxyl function of a 3-(2-aminoethylthio)-4-hydroxyalkyl-2-enenitrile as a tetrahydropyranyl derivative, this S-adduct isomerised to the corresponding N-adduct on keeping. Treatment with oxygen and sodium ethoxide in ethanol effected oxidation to the disulphide followed by amine proton abstraction and ring closure to give a 5-(1-alkyl-1-tetrahydropyranyloxyalkyl)-6-cyano-2,3-dihydro-4H-1,4-thiazine in 42% yield. Direct formation of the disulphide followed by treatment with oxygen and sodium ethoxide in ethanol gave the corresponding 5-(1-alkyl-1-tetrahydropyranyloxyalkyl)-6-cyano-2,3-dihydro-4H-1,4-thiazines in 58 to 62% yield.

Phenylpropynenitrile gave similar results with L-cysteine and cystamine. The corresponding 2,3-dihydro-

4H-1,4-thiazines were obtained in 22% and 73% yield respectively.

Three new 5,6-dihydro-3H-furo[3,4-b]-1,4-thiazines were prepared from the 5-(1-alkyl-1-tetrahydropyranyl-oxyalkyl)-6-cyano-2,3-dihydro-4H-1,4-thiazines by hydrolysis to the corresponding 5-(1-hydroxyalkyl)-6-cyano-2,3-dihydro-1,4-thiazines followed by base catalysed cyclisation.

A 2:1-bis adduct of 4-methyl-4-tetrahydropyranyl-oxyhex-2-enenitrile and bis-(2-aminomethyl-4,5-dimethoxyphenyl)disulphide was synthesised and reacted with sodium ethoxide in the absence of solvent to give 2-cyano-7,8-dimethoxy-3-(1-methyl-1-tetrahydropyranyl-oxypropyl)benzo[6,7]-thiazepine in 34% yield. The removal of the tetrahydropyranyl protecting group followed by base catalysed cyclisation gave the corresponding furo[3,4-b]benzo[6,7]-1,4-thiazepine in 65% yield.

4,4-Dialkyl-4-tetrahydropyranyloxybut-2-yne-nitriles underwent cycloaddition with acetamidine to give 6-(1-alkyl-1-tetrahydropyranyloxyalkyl)-4-amino-2-methylpyrimidines in 60 to 70% yield. These gave the corresponding 4-amino-6-(1-hydroxyalkyl)-2-methyl-

pyrimidine hydrochlorides on treatment with ethanolic hydrochloric acid in 78 to 80% yield.

2-Phenyl-4,5,5-trimethylhexa-2,3-dienenitrile similarly reacted with guanidine to give 2,4-diamino-5-phenyl-6-(1,2,2-trimethylpropyl)pyrimidine, a potential antimalarial drug, in 23% yield.

4-Hydroxy-4-methylhex-2-ynenitrile with thiourea gave 5-ethyl-5-methyl-4-(1-cyanomethylene)-2-thio-imidazolidinone in 39% yield. No trace of the corresponding pyrimidin-2-thione was observed.

The addition of half molar amounts of chiral α-phenylethylamine to two allenic nitriles resulted in the isolation of recovered allenic nitrile with low optical purity. In both cases the absolute configuration of the recovered allene was related to that of the resolving agent.