INTRAMOLECULAR REACTIONS OF ENAMINONITRILES. A NOVEL SYNTHESIS OF NEW β-AMINOPYRROLES AND RELATED HETEROCYCLES

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The report concerns novel syntheses of several new 3-aminopyrroles, 3-aminoindoles, pyrido[3,2-b]indoles and pyrrolo[3,2-b]pyridines, which have a distinctive feature involving an intramolecular addition of an enamine to a cyano group.

Enamine (I) prepared from t-butyl aminocyanoacetate and cyclohexane-1,3-dione cyclized upon substitution of the methine by ethyl bromoacetate in the presence of sodium ethoxide to afford 2-carbo-t-butoxy-2-carbethoxymethyl-3-imino-4-oxo-4,5,6,7-tetrahydroindoline. Treatment of the latter with hydrogen chloride generated a corresponding 3-aminoindole derivative. Reaction of (I) with methyl vinyl ketone (MVK)-sodium ethoxide furnished 3-amino-2-carbo-t-butoxy-4-oxo-4,5,6,7-tetrahydroindole, a product attributable to elimination of the initially introduced MVK moiety from an indoline intermediate. (I) was treated with ethyl acrylate-sodium ethoxide to obtain 2,9-dioxo-1,2,3,4,6,7,8,9-octahydro-5H-pyrido[3,2-b]indole; alcoholysis of the product gave 3-amino-2-(carboethoxyethyl)-4-oxo-4,5,6,7-tetrahydroindole.

Similarly, certain 3-aminopyrroles and 6,7-disubstituted 2-oxo-1,2,3,4-tetrahydro-5H-pyrrolo[3,2-b]pyridines have been synthesized from enamines (II) prepared from acetoacetates and t-butyl aminocyanoacetate. A steric effect of the neighbouring carbobutoxy group on the cyclization reactions has been demonstrated; enamines (III) carrying a carbethoxyl instead of the carbobutoxyl group in (II) were shown to react with MVK or acrylic acid derivatives in the presence of triethylamine or sodium ethoxide to yield 2,3,5,5-tetrasubstituted 2-pyrrolin-4-ones, products due to intramolecular attack of enamine on the ester carbonyl group. Formation of a 2-cyano-3-hydroxypyrrole compound from the latter is also dealt.

Enamines (IV) obtained by condensation of ethyl acetoacetate with aminocyanoacetamides underwent cyclizations to the expected 3-aminopyrrole-2-carboxamides, respectively upon treatment with base.

The new, substituted 3-aminopyrroles have been derived into several pyrrolo[3,2-d]- and pyrrolo[3,4-d]pyrimidines, thus disclosing new routes to the purine analogues.