Reduction of 12-acetylaminoindolo[1,2-c]quinazolines. Preparation of derivatives of the new heterocyclic system indolo[3,2-d][1,3]benzodiazepine

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Reduction of derivatives of 12-acetylaminoindolo[1,2-c]quinazoline yielded the corresponding 12-acetylamino-5,6-dihydroindolo[1,2-c]quinazolines, recyclization of which under the influence of dilute hydrochloric acid led to the formation of derivatives of the hitherto unknown system indolo[3,2-d][1,3]benzodiazepine.

It is known that several of the aminoacyl derivatives of 12-aminoindolo[1,2-c]quinazoline possess sedative properties [1]. Extending the search for biologically active compounds into the indolo[1,2-c]quinazolines, we have studied the reduction of 12-acetylaminoindolo[1,2-c]quinazolines Ia-d [2-4] by sodium borohydride in acetic acid. From the results of [5] one would expect that the amide group would here be reduced to a secondary amino group. However, we found that under these conditions 12-acetylamino-5,6-dihydroindolo[1,2-c]quinazolines (IIa-d) are formed in high yields. In other words, the C=N bond in the 1,2-position of the pyrimidine ring undergoes reduction. Reductive alkylation of the pyrimidine ring

*Deceased.

at higher temperature gives, from compound Ia, 5-ethyl-6-methyl-12-acetylamino-5,6-dihydro-
indolo[1,2-c]quinazoline (III). Compound IIIa is formed as an intermediate and this is then
acetylated under the reaction conditions with subsequent reduction of the acetyl group. An
analogous reductive alkylation of dihydropyrazinocarbazole was reported in [6].

The accessibility of 5,6-dihydroindolo[1,2-c]quinazolines opens up the possibility of
preparing compounds of a hitherto unknown series indolo[3,2-d][1,3]benzodiazepine. We have
prepared derivatives of 1(3)H-2-methyl-8H-indolo[3,2-d][1,3]benzodiazepine by recyclization
of 12-acetylamino-5,6-dihydroindolo[1,2-c]quinazolines by the action of 10% hydrochloric acid
in dioxane.

Comparing the IR spectra of the 5,6-dihydroindoloquinazolines IIIa-d with those of the
starting materials Ia-d, while the acetyl carbonyl stretching vibration band at 1670-1600
\(\text{cm}^{-1}\) is retained, a second band appears in the 3420-3320 \(\text{cm}^{-1}\) region, corresponding to the
NH group in the 5-position. In the proton NMR spectra of compounds IIIa-d a doublet from the
protons of the 6-\(\text{CH}_3\) group appears at 1.44 ppm, \(J = 6\ \text{Hz}\), and a quartet from interaction with
the 6H-protons at 6.14 ppm. In the mass spectra of the indolo[3,2-d][1,3]benzodiazepines
(IVa-d) the molecular ion peak is the maximum. The main route of decomposition of these com-
ponds, shown for compound IVa as an example, is associated with the formation of the follow-
ing fragments: \(247^* [M^+]\), \(246 [M - H]^+\), \(232 [M - \text{CH}_3]^+\), \(219 [M - \text{C}_2\text{H}_4]^+\), \(206 [M - \text{CH}_2\text{CN}]^+\),
\(205 [M - \text{CH}_3\text{CHN}]^+\), \(191 [M - \text{NHCOCH}_3]^+\), \(190 [M - \text{NH}_2\text{C}(\text{CH}_3)_2]^+\), \(179 [M - \text{CH}_2\text{CN} - \text{HCN}]^+\),
\(178 [M - \text{CH}_3\text{CHN} - \text{HCN}]^+\). The presence of the fragments \(246 [M - H]^+\) and \(219 [M - \text{C}_2\text{H}_4]^+\) is
probably explained by the existence of the indolobenzodiazepine in the tautomeric form \(A\) un-
der electron bombardment:

We suggest that the recyclization involves protonation, breaking of the pyrimidine ring,
hydrolysis with separation of acetaldehyde and cyclization of the intermediate 2-(o-amino-
aryl)-3-acetylaminoindole (V) in which the acetyl and amino groups participate.

\*Here and below, ion peaks are given \(m/z\) values.