# STRUCTURE OF THE ISOMERIZATION PRODUCT OF PERFAMINE

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UDC 547.944/945

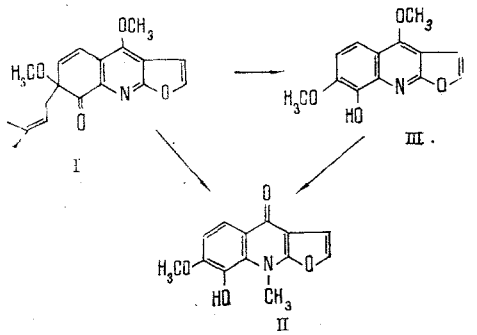
It has been shown previously that the reactivity of a methoxy group in position 4 of a furanoquinoline alkaloid depends on the structure of the homocyclic ring [1]. Thus, the conversion into N-methylfurano-4-quinolones under the action of methyliodide that is characteristic for 4-methoxyfuranoquinolines is not observed in the case of the 5,6,7,8-tetrahydrofuranoquinoline alkaloids [2].

From this point of view, it appeared of interest to study the isomerization of perfamine (I) [3], in which the homocyclic ring of the furanoquinoline nucleus is modified into a gem-substitute cyclohexadienone ring. When perfamine was heated with methyl iodide in a sealed tube for 20 h, substance (II) was formed: $C_{13}H_{11}O_4$, mp 250-252°C (decomp.), sparingly soluble in the usual organic solvents but soluble in alkali. The IR spectrum of (II) showed absorption bands at 1621, 1590, 1540, and 1500 $cm^{-1}$, which are characteristic of 4-quinolones. UV spectrum of (II): $\lambda_{max}^{C_2H_5OH}$ 212, 239, 260, 330 nm (log ε 4.14, 4.37, 4.67, 4.01), which is similar to the spectra of furano-4-quinolone compounds [4].

The fact that (II) belonged to the N-methylfurano-4-quinolone compounds was shown by its NMR spectrum taken in $CF_3COOH$. The spectrum has two pairs of 1-proton doublets, at 1.99 and 2.89 ppm (J = 10 Hz) and at 2.64 and 2.99 ppm (J = 2.5 Hz), relating to ortho-aromatic protons and the protons of a furan ring, and two three-proton singlets at 5.72 and 6.40 ppm corresponding to the protons of N-methyl and methoxy groups. These facts show the formation in the isomerization of perfamine of 8-hydroxy-7-methoxy-9-methyl-4-quinolone, which is confirmed by the results of the mass-spectrometric fragmentation of this compound.

The splitting off of the methyl radical from $M^+$ of (II) (m/e 245, 94%) and the subsequent elimination of carbon monoxide or a formyl radical gives ions with m/e 230 (100%), 202 (72%), and 201 (18%), and the splitting off of formyl radical from $M^+$ gives an ion with m/e 216 (14%). Ions with m/e 187 (50%) and 174 (40%) are formed as the result of the splitting out of a methyl radical and carbon monoxide, respectively, from the ion with m/e 202. The peaks of ions in the spectrum of (II) mentioned above are similar to those for 7-hydroxy-8-methoxy-2-methylfurano-4-quinolone (isohaplopine [5]), from which (II) differs only by the mutual positions of the OH and $OCH_3$ groups.

The chemical structure of (II) was confirmed by the preparation of 8-hydroxy-7-methoxy-2-methylfurano-4-quinolone from 8-hydroxy-4,7-dimethoxyfuranoquinoline (III), which is also formed from perfamine by acid cleavage [3].




Thus, under the conditions of heating perfamine with methyl iodide the elimination of the isopentyl substituent takes place with the formation of the phenolic compound (III) and

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 738-739, September-October, 1979. Original article submitted May 23, 1979.

 0009-3130/79/1505-0656$07.50 

the usual isomerization of a 4-methoxyfuranoquinoline derivative into a N-methylfurano-4-quinolone compound (II).

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# SYNTHESIS OF A SUBSTITUTED FRAGMENT $A^{17-21}$ OF HUMAN INSULIN


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UDC 547.964.4


In connection with the development of a new scheme for the block synthesis of the A-chain of human insulin, we have performed the synthesis of the substituted pentapeptide (I) corresponding to fragment $A^{17-21}$ of human insulin

$$\text{Bpoc-}\overset{17}{\text{Glu}}(\text{OBu}^t)\text{-Asn-Tyr}(\text{Bu}^t)\text{-Cys(Ec)-}\overset{21}{\text{Asn}}\text{-OBu}^t \qquad \text{(I)}$$

The pentapeptide (I) was synthesized by a 4 + 1 scheme using as starting materials the pentafluorophenyl ester of N-biphenylylisopropoxycarbonyl-γ-tert-butyl-L-glutamic acid (II), the pentafluorophenyl ester of $N^{\alpha}$-benzyloxycarbonyl-L-asparagine (III), the methyl ester of N-benzyloxycarbonyl-O-tert-butyl-L-tyrosine (IV), S-ethylcarbamoyl-L-cysteine (V), and the tert-butyl ester of $N^{\alpha}$-benzyloxycarbonyl-L-asparagine (VI).

Intermediate compounds were the methyl ester of O-tert-butyl-L-tyrosine (VII), the methyl ester of $N^{\alpha}$-benzyloxycarbonyl-L-asparaginyl-O-tert-butyl-L-tyrosine (III), the methyl ester of L-asparaginyl-O-tert-butyl-L-tyrosine (IX), the methyl ester of N-biphenylylisopropoxycarbonyl-γ-tert-butyl-L-glutamyl-L-asparaginyl-O-tert-butyl-L-tyrosine (X), N-biphenylylisopropoxycarbonyl-γ-tert-butyl-L-glutamyl-L-asparaginyl-O-tert-butyl-L-tyrosine (XI), the pentafluorophenyl of N-biphenylylisopropoxycarbonyl-γ-tert-butyl-L-glutamyl-L-asparaginyl-O-tert-butyl-L-tyrosine (XII), N-biphenylylisopropoxycarbonyl-γ-tert-butyl-L-glutamyl-L-asparaginyl-O-tert-butyl-O-tyrosyl-S-ethylcarbamoyl-L-cysteine (XIII), the tert-butyl ester of L-asparagine (XIV), and the pentafluorophenyl ester of N-biphenylylisoproxycarbonyl-γ-tert-butyl-L-glutamyl-L-asparaginyl-O-tert-butyl-L-tyrosyl-S-ethylcarbamoyl-L-cysteine (XV).

For the synthesis of the S-ethylcarbamoyl-L-cysteine we used the method suggested by Guttmann [1]. The pentafluorophenyl esters of N-substituted amino acids and peptides were obtained by the method of Kisfaludy et al. [2].

The protected pentapeptide (I) was purified by recrystallization from dioxane—ethyl acetate (1:10). The structure of compound (I) was determined unambiguously by the scheme of synthesis, and its individuality was checked by chromatography and the results of analytical determinations.

tert-Butyl Ester of N-Biphenylylisopropoxycarbonyl-γ-tert-butyl-L-glutamyl-L-asparaginyl-O-tert-butyl-L-tyrosyl-S-ethylcarbamoyl-L-cysteinyl-L-asparagine (I). mp 192-193°C (decomp.), $[\alpha]_D^{23}$ − 38.6° (c, 1.0; dimethylformamide). TLC on Silufol UV-254 plates; $R_f$ 0.30 (methanol—chloroform (1:9)), 0.52 (methanol—chloroform (2:17)). Found, %: C 60.49; H 7.05; N 9.87. $C_{53}H_{79}N_8O_{14}S$. Calculated, %: C 60.33; H 7.10; N 10.00. Amino acid analysis (the cysteine was not determined): Glu 1.00, Asp 1.96, Tyr 0.87.


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Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 739-740, September-October, 1979. Original article submitted April 28, 1979.

0009-3130/79/1505-0657$07.50