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S. I. GARAN, V. I. MAIMIND, Full Member of the USSR Academy of Medical Sciences S. R. MARDASHEV

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## Abstract

## Full Text

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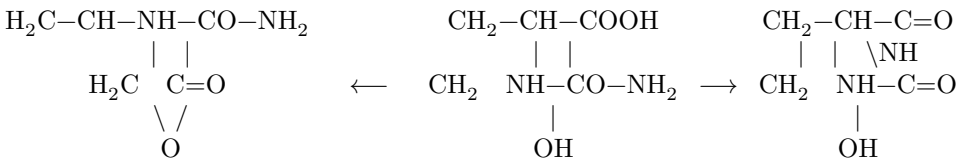
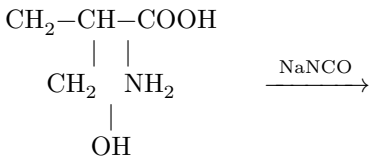
# SYNTHESIS OF THE SODIUM SALT OF CARBAMYLHOMOSERINE AND ITS AMIDE

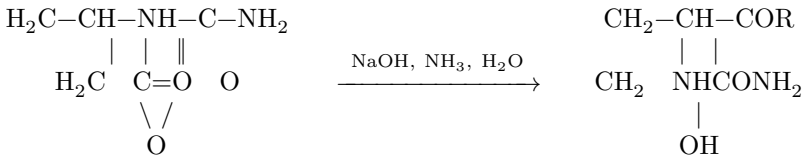
It has been shown that the first specific metabolite in the biosynthesis of nitrogenous bases of the pyrimidine series is N-carbamylaspartic acid. It seemed of interest to study the effect on the biosynthesis of pyrimidine bases of structural analogs of this compound, in particular, N-carbamylhomoserine and some of its derivatives. The synthesis of the indicated substances was the aim of the present work.

N-Carbamylhomoserine and its amide have not been described in the literature; only in the work of Livak, Britton, Vandervild, and Murray is N-carbamylhomoserine mentioned as a possible intermediate compound in the synthesis of 5-($\beta$-bromoethyl)hydantoin. It could be assumed that compounds of this kind would have the ability to cyclize very readily, giving, depending on the conditions, two series of derivatives—$\gamma$-butyrolactone and 5-($\beta$-hydroxyethyl)hydantoin:



For the synthesis of N-carbamylhomoserine and its amide, two routes were studied:

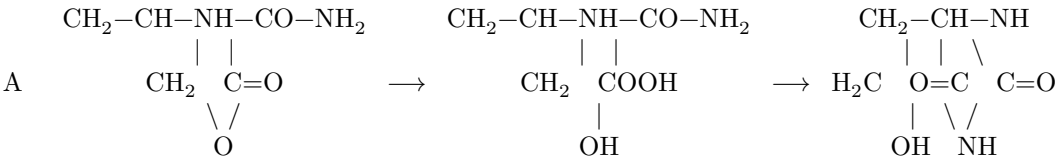


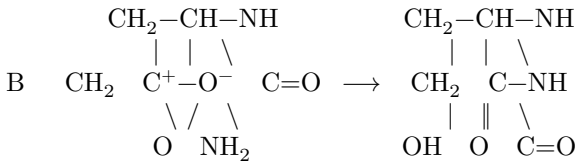



R = OH, ONa, $NH_2$

Study of the reaction of homoserine with sodium cyanate showed that, if it is carried out at room temperature with pure NaNCO at pH > 7, side reactions can be avoided and the expected Na salt of carbamylhomoserine is obtained in good yield. It was characterized by analyses and by its IR spectrum.

The amide of N-carbamylhomoserine was obtained by the second of the indicated routes. The starting $\alpha$-ureidobutyrolactone has recently been described by Rokuro Sudo ([3]) and was obtained by us under simpler conditions. It readily isomerizes under acidic conditions to a hydantoin derivative. We observed the same isomerization under the influence of temperature, for example, on heating the dry substance to the melting temperature (156-157°). The cooled melt is $\beta$-hydroxyethylhydantoin (m.p. 174-176°). As regards the mechanism of this isomerization, of the two possible variants:




Rokuro Sudo ([3]) gives preference to mechanism B. As follows from the foregoing, our data confirm the possibility of isomerization of ureidobutyrolactone without intermediate formation of the "open" form.

$\alpha$-Ureidobutyrolactone, as it turned out, readily reacts with ammonia of various concentrations with opening of the lactone ring, giving the sparingly soluble amide of carbamylhomoserine.

These results are in contradiction with the data of Frenkel and Knobler ([4]). In a recently published short communication, containing no experimental facts, they state that $\alpha$-ureidobutyrolactone is stable to the action of ammonia.

The amide of carbamylhomoserine obtained by us was characterized by analyses, including a functional analysis for the presence of an amide group, and also by an IR spectrum, and there is no doubt as to its structure.

## Experimental Part

The melting points of the compounds obtained were not corrected. The values of $R_f$ were determined on Whatman No. 1 paper, by descending chromatography in 80% phenol. The chromatograms were developed with an alcoholic solution of *n*-dimethylaminobenzaldehyde.

Sodium cyanate, free of carbonate, was obtained by the described method ([5]) by isomerization of urea in boiling dry *n*-butanol, in the presence of sodium butylate. The yield was quantitative.

**Na salt of carbamylhomoserine.** A solution of 1.52 g of homoserine and 0.865 g of NaNCO (1.04 mole) in 15 ml of water is left at room temperature overnight, after which it is evaporated in vacuo to dryness. The dense residue is triturated several times with 15 ml of absolute alcohol. Yield 85-95%, m.p. 196-197° (with decomposition; from water). The substance is very readily soluble in water, insoluble in organic solvents.

Found, %: C 32.30; H 4.91; N 15.25; Na 12.84

$C_5H_9N_2O_4Na$. Calculated, %: C 32.61; H 4.93; N 15.21; Na 12.49

$R_f$ 0.31. IR spectrum* 1763, 1737 $cm^{-1}$ (OH and NH groups); 1649 $cm^{-1}$ (CO of the ureido group); 1569 $cm^{-1}$ (ionized carboxyl).

**α-Ureidobutyrolactone.** A solution of 10 g of α-aminobutyrolactone hydrobromide and 3.64 g of NaNCO (1.03 mole) in 9 ml of water is left at room temperature for 12 hr; then it is cooled for 24 hr at 0°, and the precipitated solid is filtered off; 5.9 g–75% is obtained. From the mother liquor a further 0.67 g of substance can be isolated, which raises the total yield to 83%. M.p. 155-157° (from alcohol). $R_f$ 0.80.

IR spectrum: 1769 $cm^{-1}$ (CO of the ring); 1661 $cm^{-1}$ (CO of the ureido group).

**Amide of carbamylhomoserine.** 2 g of α-ureidobutyrolactone is dissolved in 6 ml of 23% $NH_4OH$ and left at room temperature overnight; then it is cooled for 24 hr at 0° and 1.72 g–76% is obtained. M.p. 174-176° (from water). A mixed sample with ureidobutyrolactone melts at 138-140°. On heating the amide of carbamylhomoserine in 5% NaOH for 30 min, 95.5% of amide nitrogen is liberated. The ureido group, as well as ureidobutyrolactone and the Na salt of carbamylhomoserine, are stable to hydrolysis under these conditions.

Found, %: C 37.37; H 6.89; N 25.65

$C_5H_{11}N_3O_3$. Calculated, %: C 37.26; H 6.88; N 26.07

$R_f$ 0.71. IR spectrum: 1655 $cm^{-1}$ (CO group); no bands in the region 2735-2534 $cm^{-1}$ (absence of COOH groups).

Institute of Biological and Medical Chemistry
Academy of Medical Sciences of the USSR

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* The IR spectra were taken by V. Nefedov, to whom the authors express their great gratitude.

*Note: Figure translations are in progress. See original paper for figures.*