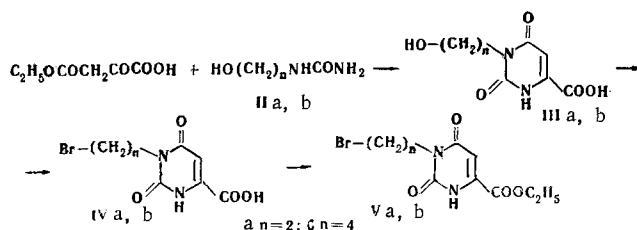


SYNTHESIS OF 3-( $\omega$ -BROMOALKYL)OROTIC ACIDS

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Continuing our investigations of the synthesis of analogs of nucleic bases [1], we have obtained 3-( $\omega$ -hydroxyalkyl)orotic acids (III) in about 40% yield by the condensation of monoethyl oxalacetate (I) with  $\omega$ -hydroxyalkylureas (II) under conditions similar to the conditions used in the synthesis of 3-methylorotic acid [2]. The presence of a hydroxyalkyl group in the 3-position of the uracil ring is confirmed by the bathochromic effect in the UV absorption spectra on passing from acid to alkaline. 3-( $\omega$ -Bromoalkyl)-orotic acids (IV) were obtained in about 80% yield by heating III at 100°C for 3 h with 48% hydrobromic acid. Their ethyl esters were synthesized by passing dry hydrogen bromide into refluxing alcohol solutions of IV for 3 h.  $\delta$ -Hydroxybutylurea (IIb) was obtained by the reaction of  $\delta$ -hydroxybutylamine with nitrourea, as in the synthesis of  $\beta$ -hydroxyethylurea [3].



## EXPERIMENTAL

3-( $\beta$ -Hydroxyethyl)orotic Acid (IIIa). This compound melted at 231-232°, solidified, and remelted at about 320° (from alcohol). Found %: C 42.0; H 4.1; N 14.2.  $C_7H_8N_2O_5$ . Calculated %: C 42.0; H 4.0; N 14.0.

3-( $\delta$ -Hydroxybutyl)orotic Acid (IIIb). This product melted at 210-212°, solidified, and remelted at about 300° (from alcohol). Found %: C 46.9; H 5.5; N 12.0.  $C_9H_{12}N_2O_5$ . Calculated %: C 47.3; H 5.3; N 12.3.

3-( $\beta$ -Bromoethyl)orotic Acid (IVa). This product melted at 220-222°. Found %: Br 30.0.  $C_7H_7BrN_2O_4$ . Calculated %: Br 30.1.

3-( $\delta$ -Bromobutyl)orotic Acid (IVb). This product melted at 181-183°. Found %: Br 26.6.  $C_9H_{11}BrN_2O_4$ . Calculated %: Br 27.4.

Ethyl 3-( $\beta$ -Bromoethyl) Orotate (Va). This compound melted at 196-196.5° (from alcohol). Found %: C 37.3; H 3.8; Br 27.7.  $C_9H_{11}BrN_2O_4$ . Calculated %: C 37.1; H 3.8; Br 27.4.

Ethyl 3-( $\delta$ -Bromobutyl) Orotate (Vb). This compound melted at 137.5-138° (from alcohol). Found %: C 41.6; H 5.1; Br 25.0.  $C_{11}H_{15}BrN_2O_4$ . Calculated %: C 41.4; H 4.7; Br 25.0.

$\delta$ -Hydroxybutylurea (IIb). This compound melted at 81-83° (from methanol). Found %: C 45.8; H 9.2; N 21.3.  $C_5H_{12}N_2O_2$ . Calculated %: C 45.4; H 8.9; N 21.2.

## LITERATURE CITED

1. A. Ya. Berlin and I. A. Korbukh, *Khim. Geterotsikl. Soedin.*, 397 (1971).
2. K. A. Chkhikvadze, N. E. Britikova, and O. Yu. Magidson, *Zh. Obshch. Khim.*, **34**, 161 (1964).
3. R. A. Charlton and A. R. Day, *J. Org. Chem.*, **1**, 1552 (1937).

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