S. I. Zav'yalov, N. A. Rodionova,
L. L. Zheleznaya, G. I. Bolestova,
V. V. Filippov, Z. N. Parnes,
and D. N. Kursanov

Previously [1] the direct synthesis of 2,3,4,5-tetradehydrobiotin (I) and its 1'-methyl derivative (II) was accomplished by starting with the ethyl ester of  $\alpha$ -ketodehydrodesthiobiotin (III). \* The ionic hydrogenation of (I) and (II) with triethylsilane in CF<sub>3</sub>COOH, as described in [3, 4], to biotin (IV) and 1'-methylbiotin (V) was studied in the present paper.



Racemic (IV) is formed in 10% yield when (I) is heated with triethylsilane in  $CF_3COOH$  (120 h, 50°C), which was identified by the mixed melting point with an authentic specimen, the NMR spectrum, and the biological activity. The ionic hydrogenation of (II) is more rapid and proceeds more smoothly. The reaction of (II) with triethylsilane in  $CF_3COOH$  (20 h, 50°) gives (V) in 30% yield. The structure of (V) agrees with its elemental analysis, NMR spectrum, and biological activity.

The presence of close signals of the protons at  $C^2$ ,  $C^3$ , and  $C^4$  in the NMR spectra of (IV) and (V) (see Experimental) and the almost identical growth-stimulating activity of (V) and (VI) [5] (Table 1) make it possible to assign the cis-configuration to (V).

TABLE 1. Growth-Stimulating Activity of (V) and cis-1-Methyldesthiobiotin (VI) toward Saccharomyces cerevisiae, in % to d-Biotin

Compound	Dose, ng/4 ml			
	0,2	0,4	0,8	1,6
(V) (VI)	34,0 36,0	19,0 23,0	9,0 8,0	5,4 4,7

## EXPERIMENTAL

The NMR spectra were taken in  $CF_3COOH$  on a DA-60-1L instrument, using HMDS as the internal standard.

 $\frac{\text{Racemic Biotin (IV).}}{\text{g of HSi}(C_2H_5)_3, \text{ and } 2.27 \text{ g of CF}_3\text{COOH was heated}}$ 

\*This synthesis scheme was described later by some Japanese authors [2], who, however, fail to refer to [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 7, pp. 1643-1644, July, 1975. Original article submitted January 8, 1975.

©1976 Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.

at 50° for 120 h, after which the mixture was evaporated in vacuo, the residue was treated with 3 ml of acetone, and the precipitate was filtered and recrystallized twice from water using activated carbon. We obtained 0.06 g (10%) of (IV), mp 216-218°. NMR spectrum ( $\delta$ , ppm): 1.30 m (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); 2.16 m (CH<sub>2</sub>CO); 2.63 s (CH<sub>2</sub>S); 3.06 m (H at C<sup>2</sup>); 4.35 m (H at C<sup>3</sup> and H at C<sup>4</sup>). The obtained (IV) failed to depress the mixed melting point with an authentic specimen, had the same NMR spectrum as the specimen, and exhibited a growth-stimulating activity toward the yeast <u>Saccharomyces cerevisiae</u> that was equal to 43% of the activity of d-biotin. The yield of (IV) in parallel experiments was 7-9%.

<u>Racemic 1'-Methylbiotin (V)</u>. A mixture of 0.2 g of (II) [1], 0.8 g of  $HSi(C_2H_5)_3$ , and 3 g of  $CF_3COOH$  was heated at 50° for 20 h, after which the mixture was evaporated in vacuo, the residue was treated with 2 ml of acetone, and the precipitate was filtered and recrystallized from water. We obtained 0.06 g (30%) of (V), mp 214-217°. NMR spectrum ( $\delta$ , ppm): 1.28 m (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); 2.10 m (CH<sub>2</sub>CO); 2.57 s (CH<sub>3</sub>N); 2.62 s (CH<sub>2</sub>S); 3.00 m (H at C<sup>2</sup>); 4.20 m (H at C<sup>3</sup> and H at C<sup>4</sup>). Found: C 51.24; H 6.88; S 12.36; N 11.08%. C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>S. Calculated: C 51.20; H 6.98; S 12.40; N 10.85%.

## CONCLUSIONS

2,3,4,5-Tetradehydrobiotin and its 1'-methyl derivative undergo ionic hydrogenation with triethylsilane in trifluoroacetic acid to respectively give biotin and 1'-methylbiotin.

## LITERATURE CITED

- 1. S. I. Zav'yalov, I. A. Rubtsov, L. L. Zheleznaya, A. B. Pavlova, and N. A. Rodionova, Izv. Akad. Nauk SSSR, Ser. Khim., 1679 (1973).
- 2. T. Taguchi, Y. Sato, K. Watanabe, and T. Mykaiyama, Chem. Letters, 729 (1974).
- 3. D. N. Kursanov and Z. N. Parnes, Usp. Khim., 38, 1783 (1969).
- 4. Z. N. Parnes, G. I. Bolestova, L. I. Belen'kii, and D. N. Kursanov, Izv. Akad. Nauk SSSR, Ser. Khim., 1918 (1973).
- 5. S. I. Zav'yalov, L. L. Zheleznaya, and A. B. Pavlova, Izv. Akad. Nauk SSSR, Ser. Khim., 1416 (1973).