This previously unrecognized phenomenon in no way influences our present conclusions and will be discussed in a full paper.

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Synthesis of α-Dehydrobiotin

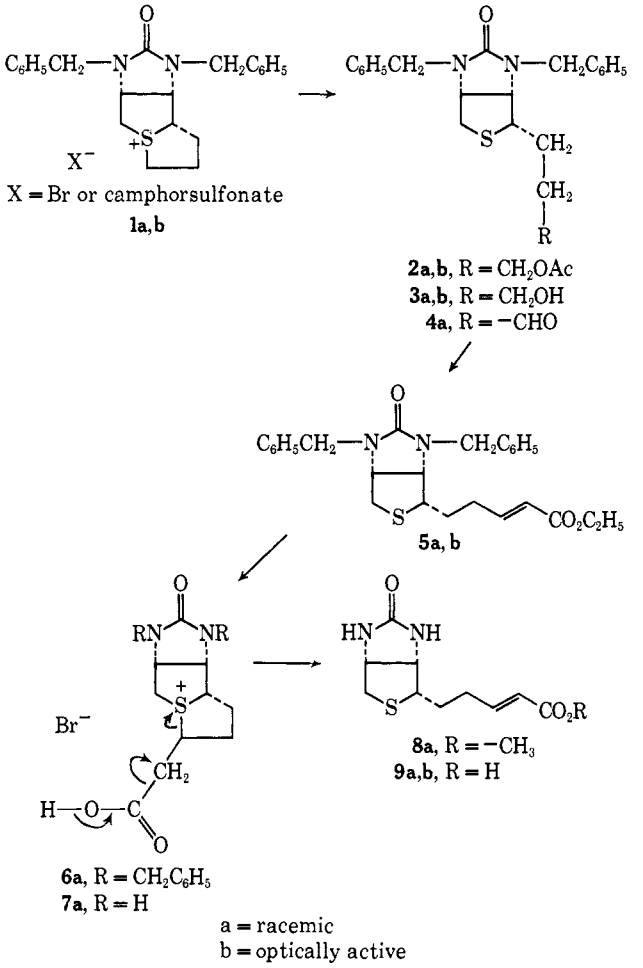
Sir:

The isolation and characterization of *d*-α-dehydrobiotin as a natural antimetabolite of the cofactor biotin with antibiotic properties against a number of microorganisms have been reported.[1] It is the most effective antimetabolite of biotin known, having about five times the potency of *d*-biotin sulfone and 80 times that of *d*-homobiotin in one assay.[1a]

This substance, which may facilitate the study of the biochemistry of biotin, was synthesized as follows. First, as a model, racemic α-dehydrobiotin was prepared by treatment of the racemic sulfonium bromide[2] **1a** with sodium acetate to give the open acetate **2** [mp 100–103°;[3] ir ($CHCl_3$) 1735 (ester C=O) and 1695 cm^{-1} (urea C=O)], which was hydrolyzed with alkali to the alcohol **3a** [mp 105–108°; ir ($CHCl_3$) 3630 (OH) and 1690 cm^{-1} (urea C=O)]. Oxidation of this alcohol to the aldehyde **4a** [mp 110–113°; ir ($CHCl_3$) 1720 (CH=O) and 1690 cm^{-1} (urea C=O); nmr ($CDCl_3$) δ 9.74 ppm (s, 1, $-CHO$)] without concomitant oxidation of the sulfide group was achieved with dicyclohexylcarbodiimide and dimethyl sulfoxide.[4] The additional two carbon atoms were attached by treatment of the aldehyde **4a** with the sodium salt of the triethylphosphonoacetate[5] to give **5a**, mp 96–100°.

Removal of the protecting benzyl groups presented unexpected problems due to the juxtaposition of the double bond and the electron-rich sulfide linkage. Heating of **5a** with 48% hydrobromic acid for 0.5 hr under reflux gave the cyclic sulfonium acid **6a** (mp 214–216°; nmr (DMSO) no band at δ 5–7 ppm); further heating under reflux for 4 hr then gave the debenzylated acid **7a**. Since it was anticipated that treatment of this intermediate with base would cause fragmentation[6] as shown by the arrows, the carboxyl group was esterified by treatment with methanol and hydrogen bromide, and then treated with sodium bicarbonate to give the methyl ester **8a**, mp 169.5–172°, which on alkaline hydrolysis gave *d,l*-α-dehydrobiotin (**9a**), mp 238–240°.

Repetition of this sequence of reactions starting from the *l*-thiophanium *d*-camphorsulfonate (**1b**) with characterization of the following optically active intermediates [**2b**, mp 98–100°, $[\alpha]^{25}D$ −50.3° (*c* 1, $CHCl_3$); **3b**, mp 85–87°, $[\alpha]^{25}D$ −54° (*c* 1, $CHCl_3$); and **5b**, mp 90–92°, nmr (DMSO) δ 5.78 (d, 1, *J* = 16 Hz, $=CH-CO_2Et$), 6.89 ppm (m, 1, $-CH=CH-CO_2Et$)] led to *d*-α-dehydrobiotin (**9b**), mp 256–257.5°, undepressed on addition of authentic material,[7] $[\alpha]^{25}D$ +105.7 (*c* 1.2, 0.1 *N* NaOH) [lit.[1] mp 238–240°, $[\alpha]^{25}D$ +92° (0.1 *N* NaOH)]. The antimicrobial properties of the synthetic material are also essentially identical with those reported[1] for the natural product.



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Thallium in Organic Synthesis. XV. Synthesis of Phenols and Aromatic Nitriles[1,2]

Sir:

We have recently reported[3] a simple, one-step synthesis of aromatic iodides which utilizes the *in situ*

(1) We gratefully acknowledge partial support of this work by the

(1) L. J. Hanka, M. B. Bergy, and R. B. Kelly, *Science*, **154**, 1667 (1967); L. J. Hanka, L. M. Reineke, and D. G. Martin, *J. Bacteriol.*, **100**, 42 (1969); (a) S. H. Rubin and J. Scheiner, *Arch. Biochem.*, **23**, 400 (1949).

(2) M. W. Goldberg and L. H. Sternbach, U. S. Patent 2,489,235 (1949).

(3) Compounds characterized by melting point gave satisfactory combustion analyses.

(4) K. E. Pfitzner and S. G. Moffatt, *J. Amer. Chem. Soc.*, **87**, 5661, 5670 (1965).

(5) W. S. Wadsworth and W. D. Emmons, *ibid.*, **83**, 1733 (1961).

(6) See C. A. Grob and P. W. Schiess, *Angew. Chem.*, **79**, 1 (1967).