1-Piperidyl-2-α-naphthylcarbamyl-3,4,6-triacetyl-D-glucose

A 7.5-g. portion of 1-piperidyl-3,4,6-triacetyl-D-glucose[1] was dissolved in 75 ml. of anhydrous pyridine. A 4.2-g. portion of α-naphthyl isocyanate was added, the flask was stoppered, and the mixture allowed to stand for an hour. At the end of this period, the flask was placed on a steam-bath for 15 minutes and then maintained at room temperature overnight. The solution was then diluted with 10 ml. of water and heated on the steam-bath for 10 minutes, whereupon it was poured into 300 ml. of ice-water. The sirup formed at this point became crystalline on maceration with 25 ml. of cold methanol. Crystallization of the crude product from 300 ml. of methanol yielded 10 g. (90%) of essentially pure product melting at 162–163°. Two additional crystallizations yielded a pure product melting at 164°, $[\alpha]^{30}D$ +36.0° (*c* 1.5, chloroform).

Anal. Calcd. for $C_{28}H_{34}O_9N_2$: C, 61.98; H, 6.34; N, 5.16. Found: C, 62.11; H, 6.49; N, 5.02.

(1) J. F. Hodge and C. E. Rist, THIS JOURNAL, **74**, 1498 (1952).

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COMMUNICATIONS TO THE EDITOR

CHARACTERIZATION OF THE ANTIBIOTIC THIOLUTIN AND ITS RELATIONSHIP WITH AUREOTHRICIN

Sir:

In 1950, the antibiotic Thiolutin was described as a neutral, optically inactive, yellow-orange crystalline elaboration product of *Streptomyces albus* to which the tentative empirical formula $C_{13}H_{14}N_3O_3S_3$ was assigned.[1] Subsequently, it became apparent that the description of aureothricin, $C_{13}H_{13}N_3O_3S_3$, previously isolated in Japan, bore much resemblance to Thiolutin.[2] Accordingly, in 1950 an interchange of samples was arranged[3] and preliminary comparisons confirmed the similarities of the two antibiotics However, recent chemical studies on Thiolutin led to the preparation of significant degradation products and their derivatives which further characterize this antibiotic and differentiate it from aureothricin. The present work invalidates the original empirical formulas of Thiolutin and aureothricin and characterizes their molecular formulas as $C_8H_8N_2O_2S_2$ and $C_9H_{10}N_2O_2S_2$, respectively.

Raney nickel desulfurization of Thiolutin in ethanol yields a white crystalline product designated "desthiolutin" (I) m.p. 130–131°. *Anal.* Calcd. for $C_8H_{14}N_2O_2$: C, 56.45; H, 8.29; N, 16.46; mol. wt., 170. Found: C, 56.78; H, 8.24; N, 16.19; mol. wt. (Rast) 187, (Signer) 160.

Cautious acid hydrolysis of Thiolutin liberates one mole of acetic acid to yield a monoamine (II), amorphous free base, m.p. 191–194° (dec.), crystalline hydrochloride hydrate salt,[4] sinters ~200°, λ^{mu}_{infl} 229, ε 5400; λ^{mu}_{max} 309, ε 6100; λ^{mu}_{max} 381, ε 11,0000. *Anal.* Calcd. for $C_6H_6N_2OS_2 \cdot HCl \cdot H_2O$: C, 29.94; H, 3.77; N, 11.64; S, 26.62; Cl, 14.72; H_2O, 7.49; neut. equiv., 240.7. Found: C, 30.22; H, 3.86; N, 11.67; S, 26.86; Cl, 15.06; H_2O, 7.62; neut. equiv., 239.5 (water–ethanol).

The amino compound (II) has been further characterized by a variety of crystalline acylated derivatives: acid succinamido compound (III) m.p. 254–255° (dec.); *Anal.* Calcd. for $C_{10}H_{10}N_2O_4S_2$: neut. equiv., 286. Found: neut. equiv., 282, 290 (dimethylformamide–water); ε-carbomethoxycaproamido compound (IV), m.p. 163.5–164°; *Anal.* Calcd. for $C_{14}H_{18}N_2O_4S_2$: mol. wt., 342. Found: mol. wt. (Rast), 339. Thiolutin is regenerated by acetylation of II, affording an especially purified preparation of the antibiotic, referred to as the acetamido derivative (V),[4,5] λ^{mu}_{max} 250, ε 6300; λ^{mu}_{max} 311, ε 5700; λ^{mu}_{max} 388, ε 11,000. *Anal.* Calcd. for $C_8H_8N_2O_2S_2$: C, 42.09; H, 3.53; N, 12.28; S, 28.07. Found: C, 42.12; H, 3.77; N, 12.19; S, 27.72. Interestingly, the propionamido derivative (VI)[4,5] is indistinguishable from aureothricin, λ^{mu}_{max} 248, ε 6100; λ^{mu}_{max} 312, ε 3900; λ^{mu}_{max} 388, ε 11,000. *Anal.* Calcd. for $C_9H_{10}N_2O_2S_2$: C, 44.61; H, 4.16; N, 11.56; S, 26.40. Found: C, 44.97; H, 4.12; N, 11.54; S, 26.40.

Thiolutin and related compounds are inherently difficult to prepare free of solvent of crystallization. The earlier observed analytical data on Thiolutin and aureothricin coincidentally approximated both the tentative C_{13} formulations and the revised formulations. The high decomposition points and low solubility of these antibiotics in camphor make direct molecular weight determinations by the Rast method unreliable. Thiolutin and aureothricin possess strikingly similar antibiotic activity and ultraviolet absorption spectra. However, present paper chromatographic methods can resolve a mixture of Thiolutin and aureothricin as well as mixtures containing other homologous acylamido deriv-

(1) F. W. Tanner, Jr., J. A. Means and J. W. Davisson, Abstracts 118th Meeting, American Chemical Society, September 7–8, 1950.

(2) (a) H. Umezawa, K. Maeda and H. Kosaka, *Japanese Medical Journal*, **1**, 512 (1948); (b) H. Umezawa, T. Tazaki, K. Maeda, H. Kosaka and S. Fukuyama, *Journal of Antibiotics (Japan)*, **2**, Suppl. A, 105 (1949); (c) K. Maeda, *ibid.*, **2**, 795 (1949); (d) K. Maeda, *Japanese Medical Journal*, **2**, 85 (1949).

(3) Aureothricin (m.p. 260–270° dec., see note 5) was obtained through the courtesy of Dr. H. Umezawa.

(4) Light absorption determined on methanol solutions.

(5) Thiolutin, aureothricin and the respective reacylated compounds V and VI decompose similarly at about 260 to 270° depending on the rate of heating.