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TWO NEW CONSTITUENTS FROM LENTINUS EDODES*

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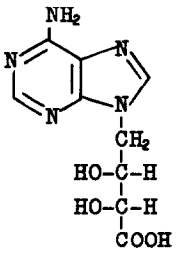
Earlier communications (1,2) have reported the structural elucidation and total synthesis of eritadenine**, 4-(6-amino-9H-purin-9-yl)-2(R), 3(R)-dihydroxybutyric acid (I), isolated as a major component from Lentinus edodes Sing. (SHIITAKE).

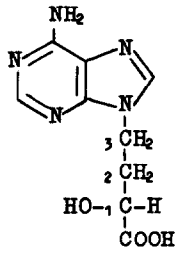
In the course of our continuing search for new consituents, we have carried out an extensive analysis of eritadenine fraction and isolated two new substances, deoxyeritadenine (II) and 4-(6-amino-9H-purin-9-yl)-propionic acid (III). The present communication deals with their structures and syntheses.

TLC of eritadenine fraction on silica gel indicated the presence of a few minor substances. Although II and III were isolated by careful preparative TLC, these compounds could be separated more satisfactorily from eritadenine as esters by the same procedure on silica gel using $CHCl_3$:MeOH (8:2). The crude eritadenine was converted to the methyl ester by treatment with MeOH and H_2SO_4. After I methyl ester was mainly removed by recrystallization, the filtrate was submitted to preparative TLC. The first minor substance, deoxyeritadenine (II), $C_9H_{11}O_3N_5$***, m.p. 270-1° (dec.), $[\alpha]_D$ +18.4°(C=1.0, 0.1N-NaOH) was closely related to eritadenine. This was evident from the similarity of spectrometric data ; $\lambda_{max}^{0.1N\text{-}HCl}$ 262mμ (ε, 13,900), $\lambda_{max}^{0.1N\text{-}NaOH}$ 262 mμ (ε, 14,300), ν_{max}(nujol) 3280, 3120 (NH_2, OH), 1700 cm^{-1} (COOH). The NMR spectrum was most informative, especially with regard to the position of the hydroxy group on the side moiety. Four protons appeared at τ 7.29 (2H, broad quartet) and τ5.72 (2H, triplet) indicating a N-CH_2CH_2 - group. One proton appeared as broad

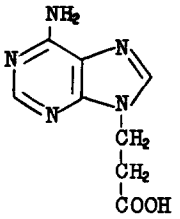
triplet at τ 6.03 is assignable to C_1-proton. From these data, deoxyeritadenine should be represented by formula II.



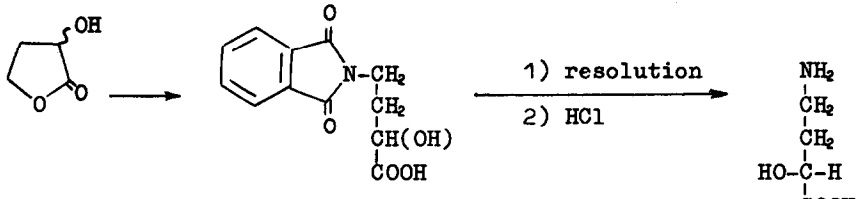
I



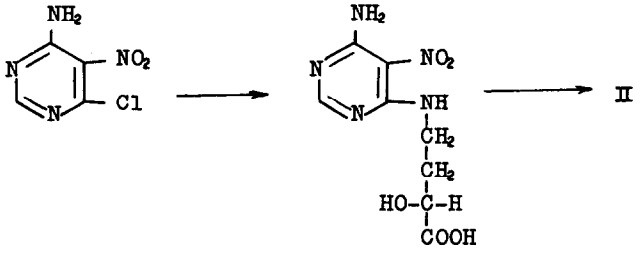
II



III



IV V



VI

The absolute configuration of the hydroxy group can be assumed to be R-configuration by analog with eritadenine. This assumption was confirmed synthetically by the method reported previously (1). Treatment of 2-hydroxybutyrolactone (3) with potassium phthalimide in DMF gave the acid (IV), $C_{12}H_{11}O_5N$, m.p. 147-8° (dec.) in 71% yield. Resolution of this acid was accomplished by conversion into its ℓ-amphetamine salt followed by recrystallization from EtOH. Hydrolysis of an optical pure salt, $C_{21}H_{24}O_5N_2$, m.p. 155-6°, $[\alpha]_D$ -4.5° (C=5.0, H_2O) with 6 N-HCl yielded the amino acid (V) $C_4H_9O_3N$, m.p. 199-201° (dec.),

$[\alpha]_D$ +27.5° (C=1.0, H_2O) in good yield.

In order to have an evidence concerning the configuration, V was converted to the corresponding lactone by treatment with $NaNO_2$ in dil. AcOH. This lactone (4), b.p. 101-3° (3 mm), $[\alpha]_D$ +20.36° (C=8.8, H_2O) showed a nagative Cotton effect (5.6), CD;$\Delta\varepsilon_{218}$-1.6 (1N-HCl). From the above result, the configuration of V should undoubtedly be assigned as R-configuration.

Condensation of V with 4-amino-6-chloro-5-nitropyrimidine gave the nitro acid (VI), $C_8H_{11}O_5N_5$, m.p. 236-7° (dec.), $[\alpha]_D$ +26.0° (C=1.0, 0.1N-NaOH) in 95% yield. Reduction of VI with Pd-C in HCOOH followed by treatment with NaOH afforded 4-(6-amino-9H-purin-9-yl)-2(R)-hydroxybutyric acid (II), $C_9H_{11}O_3N_5$, m.p. 269° (dec.), $[\alpha]_D$ +17.0° (C=1.0, 0.1N-NaOH) in 94% yield. This synthetic sample was identical with the natural deoxyeritadenine in all respects.

The second new substance (III), $C_8H_9N_5O_2$, m.p. 277-8° (dec.), $\lambda_{max}^{0.1N\text{-}HCl}$ 259 mμ (ε, 13,800), $\lambda_{max}^{0.1N\text{-}NaOH}$ 262mμ (ε, 14,400) was isolated in very minute quantities. This compound is also closely related to I and II. The NMR spectrum showed two triplets at τ7.10 (2 H) and τ5.61 (2 H) indicating as ethylene group. From these data, the second compound must have the structure III. This structure was verified by comparison with the authentic specimen which was synthesized from adenine and ethyl acrylate according to Lira's procedure (7).

Details of this work will be reported in future.

References

* This work was presented at the 90th Annual Meeting of the Pharmaceutical Society of Japan at Sapporo, July 1970 (Meeting Abstracts, p. II-155).

** Although it has been named as lentysine (1) or lentinacin (2), both groups have agreed to use the name "eritadenine".

*** Satisfactory elemental analyses were obtained for all the new compounds described in this communication. All melting points and boiling point are uncorrected.

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