and the residue extracted into chloroform. The extract was washed with dilute potassium iodide solution, then with water, and, after drying, it was concentrated to a sirupy residue. The residue was dissolved in 200 ml. of 95% ethanol, treated with 20 ml. of concd. hydrochloric acid, and refluxed for 1.5 hr., whereupon methyl mercaptan evolved. After the reflux period, the solution was concentrated slightly, causing precipitation of 2.6 g. (30%) of crude V. A sample for analysis, recrystallized from ethyl acetate, had a m.p. of 191–194°.

Anal. Calcd. for $C_{29}H_{23}N_3O_9$: C, 62.47; H, 4.16; N, 7.55. Found: C, 62.02; H, 4.11; N, 7.53.

6-Azauridine (VI).—A solution of 590 mg. (1.06 mmoles) of V in 200 ml. of methanol, saturated at 5° with ammonia, was held for 3 days at room temperature. After concentration to dryness, the residual sirup was dissolved in water and the solution was washed with ether. The aqueous solution was concentrated to dryness and the residue dissolved in absolute ethanol and reconcentrated. This operation was repeated several times to assure removal of water. Recrystallization of the residue from absolute ethanol afforded 160 mg. (62%) of 6-azauridine (VI); m.p. 157–159°, undepressed by biosynthetic material. The infrared spectrum was identical to that of authentic material as was the ultraviolet spectrum: $\lambda_{max}^{0.2\ N\ NaOH}$ 257 mμ (ε 6988).

Anal. Calcd. for $C_8H_{11}N_3O_6$: C, 39.19; H, 4.52; N, 17.14. Found: C, 39.79; H, 4.56; N, 17.34.

Acknowledgment.—The authors wish to thank Dr. E. T. Stiller and Mr. M. A. Dolliver for their continuing interest in this work. They are also indebted to Dr. J. Bernstein for helpful discussions and consultations.

2,4-Dinitrothiazole. The Boron Trifluoride–Nitrogen Tetroxide Nitration of 2-Nitrothiazole

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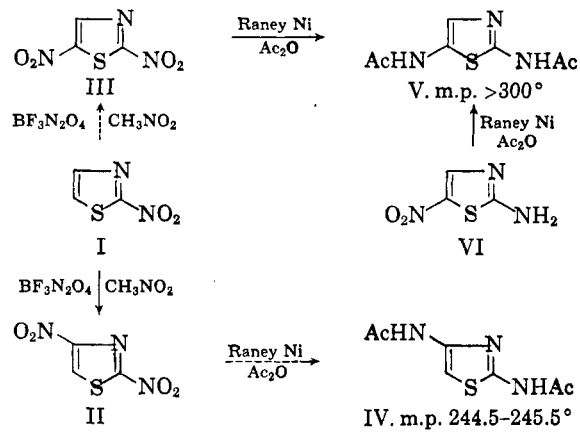
The only C-dinitrothiazoles that have been reported are 2,4-dinitro-5-acetamidothiazole,[1] and 2 - nitramino - 3,4,5 - trinitro - 2 - thiazoline.[2] Ganapathi,[3] however, has presented data that place the structure of the former compound in considerable doubt. In fact, his evidence indicates that this compound is indeed the mononitrothiazole (5-acetamido-4-nitrothiazole). In contrast to the work of Prijs,[4] we have found that 2-nitrothiazole (I) can be nitrated in excellent yield using a complex of boron trifluoride and nitrogen tetroxide.[5] It is curious to note however, that the nitration which is described below, does not proceed satisfactorily unless an excess of boron trifluoride is present in the nitration mixture.[6]

Two isomers are possible from the nitration of 2-nitrothiazole: 2,4-dinitro-(II) and 2,5-dinitrothiazole (III). Since the corresponding acetylated



diamines (IV and V) of the two possible products (II and III) were known,[7–9] the reduction of the dinitro compound seemed the best means of identification. Using 2-amino-5-nitrothiazole (VI) as a model compound, several chemical reductions were attempted in vain. Ultimately, reductive acetylation with Raney nickel catalyst was successful. Contrary to the experience of Ganapathi,[7] this reduction proceeded smoothly yielding the previously described[7] 2,5-diacetamidothiazole (V). When the nitration product (II) was subjected to this same procedure, 2,4-diacetamidothiazole (IV) resulted. This was identified by a mixed melting point determination and comparison of the infrared spectrum with that of an authentic sample prepared according to Davies.[9]

Experimental

2,4-Dinitrothiazole (II).—A stirred solution of 10 ml. of nitrogen dioxide–nitrogen tetroxide (Matheson) in 25 ml. of nitromethane was cooled to 0°, and boron trifluoride gas was bubbled in until dense white fumes were evolved from the condenser. A solution of 2 g. of 2-nitrothiazole[4] (m.p. 74–75°) in 25 ml. of nitromethane was added portionwise with stirring, and the mixture was refluxed for 1 hr. The mixture was then filtered hot, the solids washed with 25 ml. of nitromethane, and the solvent removed by evaporation in a stream of air. The yield was 2.60 g. Crystallization from benzene afforded 2,4-dinitrothiazole (m.p. 145.5–146.5° corr.) in 80% yield.

Anal. Calcd. for $C_3HN_3O_4S$: C, 20.59; H, 0.57; N, 24.00. Found: C, 20.84; H, 0.59; N, 24.25.

Reductive Acetylation of 2-Amino-5-nitrothiazole (VI).—

(1) B. Prijs, W. Menigisen, S. Fallab, and H. Erlenmeyer, *Helv. Chim. Acta*, **35**, 187 (1952).

(2) S. J. Viron and A. Taurins, *Can. J. Chem.*, **31**, 885 (1953).

(3) K. Ganapathi and K. D. Kulkarni, *Proc. Indian Acad. Sci.*, **37A**, 758 (1953).

(4) B. Prijs, J. Ostertag, and H. Erlenmeyer, *Helv. Chim. Acta*, **30**, 1200 (1947).

(5) G. B. Bachman, H. Feuer, B. R. Bluestein, and C. M. Vogt, *J. Am. Chem. Soc.*, **77**, 6188 (1955).

(6) Bachman's nitration procedure involves filtering and pressing the solid complex on a porous plate, thus any excess boron trifluoride dissolved in the solvent is removed.

(7) K. Ganapathi and A. Venkataraman, *Proc. Indian Acad. Sci.*, **22A**, 343 (1945).

(8) K. Ganapathi and A. Venkartaraman, *Proc. Indian Acad. Sci.*, **22A**, 359 (1945).

(9) W. Davies, J. A. Maclaren, and L. R. Wilkinson, *J. Chem. Soc.*, 3491 (1950).

Five grams of 2-amino-5-nitrothiazole (VI) (m.p. 200–201°) was added to sufficient acetic anhydride (about 300 ml.) to effect solution. Approximately 0.5 g. of Raney nickel[10] was added, and the mixture was shaken at 40 p.s.i. of hydrogen for 3 hr. with no observed pressure drop. Additional portions of catalyst were added periodically until the theoretical pressure drop was recorded. (A total of four portions was added over a period of 2 days). The slurry was filtered and the solids were extracted with hot acetic acid. A 65% yield of 2,5-diacetamidothiazole V (4.46 g.) m.p. > 300° (lit., m.p.[7] > 285°) was obtained by evaporation of the acetic acid extracts. This product can be recrystallized from acetic acid–water mixtures.

Anal. Calcd. for $C_7H_9N_3O_2S$: C, 42.20; H, 4.53; N, 21.05. Found: C, 42.47; H, 4.28; N, 21.16.

Reductive Acetylation of 2,4-Dinitrothiazole.—The procedure followed here was that described in the previous example, but the isolation procedure was slightly different because of the solubility of the product in acetic anhydride. After reduction was complete, the catalyst was filtered, the acetic anhydride removed under vacuum, and the residue was recrystallized from hot water. From 5 g. of dinitrothiazole, 4.95 g. (87% yield) of product (m.p. 244.5–245.5° corr.) (lit.,[9] m.p. 240–241°) were obtained.

Anal. Calcd. for $C_7H_9N_3O_2S$: C, 42.20; H, 4.53; N, 21.05. Found: C, 42.42; H, 4.60; N, 20.75.

Acknowledgment.—The author is indebted to J. J. Kobliska and his associates for the microanalyses and to Miss J. L. Gove for the infrared spectra.

(10) Prepared according to L. Covert and H. Adkins, *J. Am. Chem. Soc.*, **54**, 4116 (1932).

A Flavopereirine Synthesis[1]

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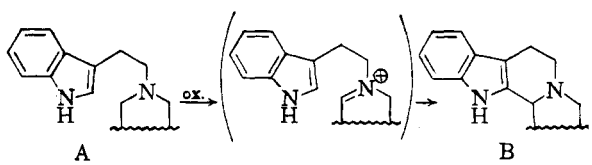
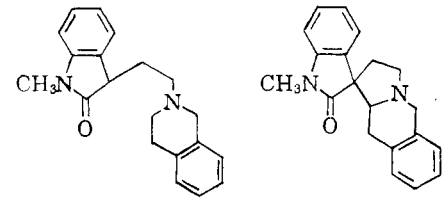
As part of a general search for new methods of synthesis of indole alkaloids the scheme outlined below (A→B) came under consideration. While two procedures were developed, one using mercuric acetate as the oxidizing agent[1] and the other palladium, the latter is the subject of this communication.



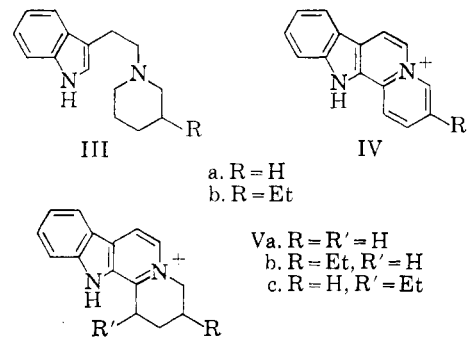
A B

It was decided to model our oxidative cyclization after the strikingly elegant and simple, but unapplied example of a palladium-induced conversion of the oxindole derivative I into II.[3] However, since substances of general type B are known to undergo palladium-catalyzed dehydrogenation,[4] the final products were expected to be anhydronium compounds, tetradehydro and octadehydro derivatives of B.



I II

Exposure of the hydrochloride of *N*-[β-(3-indolyl)ethyl]piperidine (IIIa)[5] to palladium-charcoal at 300° for twenty minutes and conversion of the products to salts led to the anhydronium in compounds IVa and Va. A similar treatment of 1[β-(3-indolyl)-ethyl]-3-ethylpiperidine (IIIb)[6] yielded the salts of flavopereirine (IVb), tetrahydroflavopereirine (Vb), and tetrahydroisoflavopereirine (Vc).



III IV

a. R = H
b. R = Et

Va. R = R′ = H
b. R = Et, R′ = H
c. R = H, R′ = Et

The last reaction constitutes a novel and short synthesis of flavopereirine, one of the alkaloids of the bark of *Geissospermum vellosii* and *laeve*.[7]

Experimental

Dehydrogenations.—A solution of 500 mg. of the piperidinoindole in a minimum amount of methanol was saturated

(1) This work was first presented as one part of a lecture by E. W. at the 17th National Organic Symposium of the American Chemical Society at Bloomington, Ind., June 26–29, 1960. The authors acknowledge gratefully hereby the financial support of the work by a Public Health Service Grant (MY-5815) from the U. S. Department of Health, Education, and Welfare.

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(4) *Cf.* E. Wenkert and D. K. Roychaudhuri, *J. Am. Chem. Soc.*, **80**, 1613 (1958).

(5) R. C. Elderfield, B. Fischer, and J. M. Lagowski, *J. Org. Chem.*, **22**, 1376 (1957).

(6) Compounds IIIb and Vc were prepared previously by Dr. B. Wickberg[1] in connection with another study.

(7) (a) M.-M. Janot, R. Goutarel, A. LeHir, and L. O. Bejar, *Ann. pharm. France*, **16**, 38 (1958). (b) H. Rapoport, T. P. Onak, N. A. Hughes, and M. G. Reinecke, *J. Am. Chem. Soc.*, **80**, 1601 (1958). (c) N. A. Hughes and H. Rapoport, *ibid.*, **80**, 1604 (1958). (d) A. Bertho, M. Koll, and M. I. Ferosie, *Chem. Ber.*, **91**, 2581 (1958). For previous syntheses see (e) A. LeHir, M.-M. Janot, and D. van Stolk, *Bull. soc. chim. France*, 551 (1958). (f) K. B. Prasad and G. A. Swan, *J. Chem. Soc.*, 2024 (1958). (g) J. Thesing and W. Festag, *Experientia*, **15**, 127 (1959). (h) H. Kaneko, *J. Pharm. Soc. Japan*, **80**, 1374 (1960). (*i*) Y. Ban and M. Seo, *Tetrahedron*, **16**, 5 (1961).