of 0.6301 N aqueous sodium hydroxide (15.73 mmoles) was added a solution of 3.70 g (15.48 mmoles) of N-ethyl-2-ethoxypyridinium fluoroborate in 20 ml of water. Water was then added to bring the volume to 100 ml and the system was stirred, under nitrogen, at 27° for 11 hr. The product was saturated with sodium chloride and exhaustively extracted with methylene chloride, and the extracts were dried. After concentrating by distillation the residue was subjected to gas chromatographic analysis;[6] 1.37 g (89% yield) of N-ethyl-α-pyridone was found and no 2-ethoxypyridine could be detected.

B. With Sodium Iodide.—A solution of 3.34 g of I in 50 ml of acetone was treated with 2.10 g of sodium iodide. The resulting light yellow solution was protected from light and stirred under nitrogen at 27°. After 119 hr the reaction was 84% complete. Vpc analysis[6] revealed the presence of N-ethyl-α-pyridone; no 2-ethoxypyridine could be found even though as little as 0.2% could readily be detected. On working up the product 0.86 g (68% yield) of a colorless oil, bp *ca.* 90° (1 mm), was isolated; its infrared spectrum was identical with that of authentic N-ethyl-α-pyridone.

C. With Sodium Ethoxide.—To 55 ml of 0.023 N sodium ethoxide in DMSO was added 0.303 g of I dissolved in 25.0 ml of DMSO. Additional DMSO was added until the final volume was 100 ml and the system was stirred, under nitrogen, at 29° for 1.5 hr. On working up the product and analyzing by vpc, methylene chloride, DMSO, and N-ethyl-α-pyridone were found, but 2-ethoxypyridine could not be detected.

Reaction of the Sodium Salt of α-Pyridone and Triethyloxonium Fluoroborate.—The following is a typical example of the reactions described in Table I. A three-necked, round-bottom flask was equipped with a Trubore stirrer, a pressure equalizing funnel, and an adapter containing a gas inlet tube and thermometer; the assembly was flamed under nitrogen. To the flask was added 2.72 g (23.20 mmoles) of the sodium salt of α-pyridone and 60 ml of methylene chloride. The slurry was stirred and cooled to −3.5° with an ice–salt bath. In 20 ml of methylene chloride was dissolved 4.42 g (23.20 mmoles) of triethyloxonium fluoroborate; the solution was cooled to −5° and added rapidly to the sodium salt. Within 1 min the temperature rose to 2°. After 5 min at 2° the mixture was filtered into 10 ml of water. Titration with aqueous sodium hydroxide showed no acid; the oxonium salt had all reacted. The salts were thoroughly washed with methylene chloride, dissolved in water, and titrated for unreacted sodium salt of α-pyridone using 0.100 N hydrochloric acid (53.30 ml of acid required). To the resulting neutral, aqueous solution was added 50 g of potassium acetate in 20 ml of water. After 12 hr at 0° 2.07 g (16.4 mequiv) of potassium fluoroborate was collected by filtration.

The methylene chloride solution was extracted with 75 ml of water and four 25-ml portions of water, dissolved methylene chloride was removed by evaporation, and the aqueous extract (cooled to 0°) was treated with a freshly prepared solution of 2.5 g of sodium tetraphenylboron in 25 ml of water. After 10 min at 0°, 2.48 g (29% yield) of N-ethyl-2-ethoxypyridinium tetraphenylboron, mp 148.5–149.5°, was obtained. Recrystallization from 95% ethanol gave white crystals, mp 153–154°; the infrared spectrum was identical with that of an authentic sample. To the aqueous filtrate was added a solution of 5 g of potassium chloride in 25 ml of water and the resulting precipitate of potassium tetraphenylboron was removed by filtration. The clear, aqueous filtrate was saturated with sodium chloride and exhaustively extracted with methylene chloride. These extracts were combined with the original methylene chloride solution, dried, and concentrated by distillation at atmospheric pressure to a volume of *ca.* 25 ml. Analysis[6] by vpc gave 0.47 g (21% yield) of 2-ethoxypyridine and 0.88 g (40% yield) of N-ethyl-α-pyridone.

Reaction of the Sodium Salt of α-Pyridone with N-Ethyl-2-ethoxypyridinium Fluoroborate (I).—A solution of 3.59 g of I in 20 ml of methylene chloride was added to a slurry of 1.76 g of the sodium salt of α-pyridone in 60 ml of methylene chloride. The mixture was stirred under nitrogen at 25° for 48 hr with protection from light. The solid was isolated by filtration, dissolved in water, and titrated with 0.100 N hydrochloric acid, requiring 72.40 ml. Treatment with sodium tetraphenylboron (*vide supra*) yielded 4.21 g of white crystals, mp 152–153°; thus the reaction was 40% complete. Recrystallization from 95% ethanol gave crystals, mp 154–155°, having an infrared spectrum identical with that of authentic N-ethyl-2-ethoxypyridinium tetraphenylboron.

Further work-up (*vide supra*) yielded a concentrate which by vpc analysis[6] was found to contain 0.14 g (9% yield) of 2-ethoxypyridine and 1.18 g (79% yield) of N-ethyl-α-pyridone.

Stability of 2-Ethoxypyridine and of N-Ethyl-α-pyridone to N-Ethyl-2-ethoxypyridinium Fluoroborate (I).—2-Ethoxypyridine (0.90 g, 7.30 mmoles) was dissolved in 50 ml of methylene chloride and treated with a solution of 1.75 g of I in 30 ml of methylene chloride. The solution (protected from light) was stirred under nitrogen at 25° for 4 days. At the end of this time the dialkylate I was recovered quantitatively as the tetraphenylboron salt (3.43 g, mp 152–153°). Recrystallization from 95% ethanol gave white crystals, mp 154–155°; the infrared spectrum was the same as that of authentic tetraphenylboron salt of I. The remainder of the product gave a concentrate (*vide supra*) which by vpc analysis[6] was found to contain 0.82 g (91% recovery) 2-ethoxypyridine. No N-ethyl-α-pyridone was found; 1.5% could readily be detected.

In the same way, equivalent amounts of N-ethyl-α-pyridone and I were allowed to react for 4 days at 25°; the reactants were quantitatively recovered and no 2-ethoxypyridine could be detected by vpc.

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The Absolute Configuration of *trans*-2,6-Dimethylpiperidine[1]

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Among the naturally occurring simple piperidine derivatives are (−)-2,6-dimethylpiperidine (I) and its N-methyl derivative, (−)-1,2,6-trimethylpiperidine (II), whose isolation from *Nanophyton erinaceum* was reported by Kuzovkov and Menshikov[2] in 1950. These simple compounds possess many of the structural features common to more complex piperidine alkaloids, such as pinidine, carpaine, cassine, and the hemlock and lobelia alkaloids. As part of our continuing study of the stereochemistry of natural piperidines,[3] we have determined the absolute configurations of I and II.

The configurations were established by Hofmann degradation of both enantiomers of II to 2-dimethylaminoheptane, whose configuration was then related to that of 2-heptanol.

A mixture of *cis*- and *trans*-(±)-I, prepared by sodium–alcohol reduction of 2,6-lutidine, was carefully separated by fractional distillation. The pure *trans*-I obtained was methylated under Eschweiler–Clark conditions to *trans*-II, and this was partially resolved[4] with *d*-tartaric acid to give dextrorotatory II. Hofmann elimination of the methiodide of (+)-II yielded 2-dimethylaminohept-6-ene (III), which was hydrogenated to (+)-2-dimethylaminoheptane (IV), characterized as its crystalline levorotatory methiodide.

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(2) A. D. Kuzovkov and G. P. Menshikov, *Zh. Obshch. Khim.*, **20**, 1524 (1950); *Chem. Abstr.*, **45**, 2485 (1951).

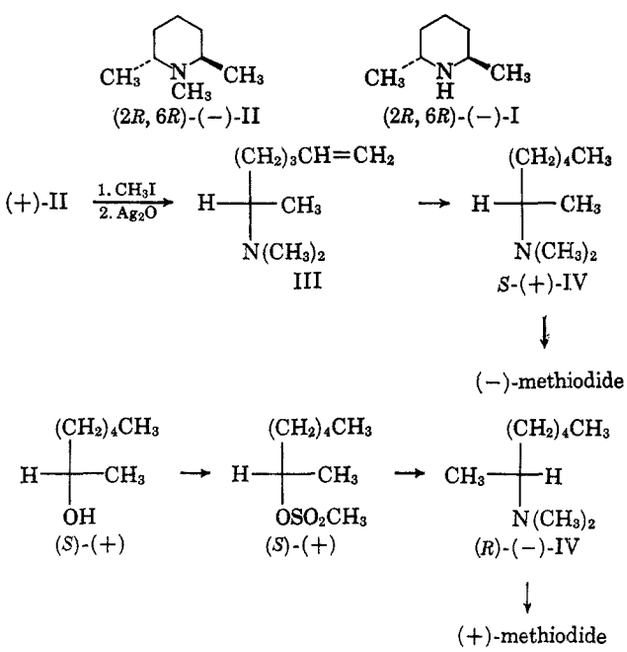
(3) R. K. Hill, T. H. Chan, and J. A. Joule, *Tetrahedron*, **21**, 147 (1965), and references therein.

(4) R. Lukeš and J. Jizba, *Collection Czech. Chem. Commun.*, **19**, 930 (1954).

Repetition of the sequence with (−)-II gave (−)-IV.

To determine the absolute configuration of IV, (*S*)-(+)-2-heptanol[5] was converted to the mesylate and treated with dimethylamine to afford, *via* Walden inversion, (*R*)-(−)-IV.

These correlations establish the configuration of natural(−)-II as (2*R*:6*R*). Since Kuzovkov and Menshikov[2] showed that both *Nanophyton* bases belong to the same configurational series by methylating (−)-I to (−)-II, both levorotatory bases have the (*R*) configuration at both asymmetric centers, as shown.



Experimental Section

trans-2,6-**Dimethylpiperidine** (*dl*-**I**).—A mixture of *cis*- and *trans*-2,6-dimethylpiperidines was prepared by sodium–ethanol reduction of 2,6-lutidine, following the literature procedure.[3,6] Repeated distillation of the mixture through an 18-in. spinning-band column gave pure *trans*-I, bp 136–138° (lit. bp 133–134°, 136–137°). Vpc analysis showed the absence of the *cis* isomer.

The **hydrochloride** was recrystallized from ethyl acetate–ethanol and melted at 236–238° (lit.[3,6] mp 232–234°, 240–242°).

Anal. Calcd for $C_7H_{16}ClN$: C, 56.18; H, 10.78; N, 9.36. Found: C, 56.21; H, 10.82; N, 9.18.

trans-**1,2,6-Trimethylpiperidine** (*d,l*-**II**).—To a cooled solution of 30.4 g of 90% formic acid and 22.2 g of 37% aqueous formaldehyde solution was added 26.8 g of racemic I. The mixture was refluxed for 12 hr, treated with 20 ml of concentrated hydrochloric acid, and heated on the steam bath for several hours. The solution was made basic with 20% sodium hydroxide and extracted with ether. After drying, distillation gave 22.7 g of *dl*-II, bp 154–155° (lit.[2,4] bp 151.5°, 153–154°).

The **picrate** was recrystallized from water and melted at 255.5–257° dec (lit.[4] mp 244–245° dec).

Anal. Calcd for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.35; H, 5.75; N, 15.61.

The **methiodide**, after recrystallization from ethanol, melted at 324–325° dec (lit.[4] mp 313° dec).

Anal. Calcd for $C_9H_{20}IN$: C, 40.16; H, 7.49; N, 5.20. Found: C, 40.17; H, 7.67; N, 5.31.

Partial Resolution of *dl*-**II.**—To a nearly saturated solution of 23.6 g of *d*-tartaric acid in hot ethanol was added 20 g of *dl*-II and the resulting solution was cooled overnight. The salt obtained (26 g) was repeatedly recrystallized from ethyl acetate–ethanol until the weight dropped to 5 g. This salt was dissolved in water, made alkaline with 20% sodium hydroxide, and extracted with ether. Concentration of the dried ether solution gave 1.8 g of II, $[\alpha]^{23}D$ +7.7° (neat, 1-dm tube). Since the naturally occurring enantiomer has $[\alpha]D$ −43.02° (neat, 1-dm tube),[2] the partially resolved base is about 18% optically pure.

The **methiodide**, recrystallized from ethanol, melted at 318–320° dec.

Anal. Calcd for $C_9H_{20}IN$: C, 40.16; H, 7.49; N, 5.20. Found: C, 40.12; H, 7.46; N, 5.25.

Hofmann Elimination of (+)-**II. A.**—The Hofmann elimination was carried out as described[4] for *dl*-II. A suspension of silver oxide (from 1.63 g of silver nitrate) in 17.5 ml water was stirred with 1.35 g of the methiodide of (+)-II in the dark for 5 hr. The mixture was filtered, the filtrate was concentrated *in vacuo*, and the residue was heated at 100° at 18 mm. The distillate was treated with potassium carbonate and extracted with ether; concentration of the dried ether solution left 0.28 g of 2-dimethylaminohept-6-ene (III). This substance was not characterized, except for the infrared bands at 915 and 997 cm^{-1}, consistent with the structure assigned by Luleš and Jizba.[4]

III was taken up in 5 ml of ethanol and 0.2 ml of concentrated hydrochloric acid and hydrogenated over 5% palladium–charcoal. Filtration and concentration of the filtrate gave 0.32 g of solid hydrochloride. Since repeated recrystallization of this hydrochloride did not give material with a satisfactory analysis, it was converted to the **methiodide of IV**, mp 195.5–196.5°, recrystallization from ethanol, $[\alpha]^{24}D$ −4.7° (*c* 1.3, chloroform).

Anal. Calcd for $C_{10}H_{24}IN$: C, 42.11; H, 8.48; N, 4.99. Found: C, 42.38; H, 8.81; N, 4.88.

B.—(−)-II was recovered from the mother liquors of the resolution, and the Hofmann elimination and subsequent hydrogenation were carried out as above on 2 g of II, $[\alpha]^{24}D$ −2.0° (neat, 1-dm tube). The 2-dimethylaminoheptane (IV) produced had $[\alpha]^{22}D$ −0.3° (neat, 1-dm tube), and an infrared spectrum identical with that of authentic IV.

Preparation of 2-Dimethylaminoheptane (IV) from 2-Heptanol.—2-Heptanol was resolved by the procedure of Kenyon and Walch,[7] giving material, bp 77–78° (24 mm), $[\alpha]^{25}D$ +7.3° (*c* 13.5, ethanol) [lit.[8] bp 73.5° (20 mm), $[\alpha]^{20}D$ +10.32°]. This was converted to the methanesulfonate, bp 75–76° (0.1 mm), $[\alpha]^{23}D$ +6.9° (neat, 1-dm tube) [lit.[9] bp 77–79° (1 mm), $[\alpha]^{25}D$ +20.96° (neat, 2-dm tube)].

The methanesulfonate (4.0 g) and dimethylamine (2.9 g) in 10 ml of benzene were heated in a pressure bottle at 90–100° for 12 hr. The reaction mixture was partitioned between benzene and dilute hydrochloric acid and the aqueous phase extracted several times with benzene. The aqueous layer was made basic with potassium carbonate and extracted with ether; after drying, distillation gave 1.3 g of 2-dimethylaminoheptane (IV), bp 56–58° (17 mm) (lit.[10] bp 160–163°), $[\alpha]^{22}D$ −2.6° (neat, 1-dm tube), $[\alpha]^{25}D$ +1.4° (*c* 0.75, ethanol, this rotation was obtained on a Cary 60 ord instrument).

The **methiodide**, after recrystallization from ethanol, melted at 195–196°, $[\alpha]^{24}D$ +11.5° (*c* 0.87, chloroform). The infrared spectrum was identical with that of the methiodide from Hofmann degradation of II.

Anal. Calcd for $C_{10}H_{24}IN$: C, 42.11; H, 8.48; N, 4.99. Found: C, 42.13; H, 8.74; N, 4.91.

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Citrus Carotenoids. V. The Isolation of 8′-Hydroxy-8′,9′-dihydrocitranaxanthin

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In a previous communication,[2] we have described the isolation and structure determination of a new carot-

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