A mixture melting point with an authentic sample of α-pipecoline hydrochloride[37] showed no depression. One gram of the above product was converted to the free base, and a picrate was prepared in the usual manner. After recrystallization from acetone–ether the yellow crystalline picrate melted at 130–132°.

Anal. Calcd. for $C_{12}H_{16}N_4O_7$: C, 43.90; H, 4.91; N, 17.07. Found: C, 43.69; H, 5.13; N, 16.69.

The mixture melting point with the picrate of authentic α-pipecoline[37b] was 131–133°.

Quaternary Salts of Conidine (Table IV).—Conidine methyl bromide, ethyl bromide, methyl iodide and ethyl iodide were prepared by treating at room temperature ethereal solutions of conidine with a slight excess of the appropriate alkyl halide. The products did not crystallize easily. In each case it was necessary to remove the ether *in vacuo* and treat the oily residue with hot acetone or ethanol. The salts usually crystallized immediately on cooling to room temperature with or without the addition of ether or ethyl acetate. These quaternary salts were all hygroscopic.

4-Iodobutyltrimethylammonium Iodide.[38]—Trimethylamine was bubbled slowly through a solution of 80 g. (0.26 mole) of tetramethylene diiodide in 150 ml. of benzene at room temperature until 10 g. (0.17 mole) had been absorbed. The mixture was allowed to stand at room temperature for 48 hours, and then the crystalline precipitate was collected and recrystallized from isopropyl alcohol; m.p. 167–167.5° dec., yield 41 g. (42.8%).

Anal. Calcd. for $C_7H_{17}NI_2$: C, 22.78; H, 4.64; N, 3.80. Found: C, 22.95; H, 4.58; N, 4.00.

N-(4-Dimethylamino-*n*-butyl)-conidinium Iodide Methiodide (Table IV).—A solution of 4 g. (0.036 mole) of conidine and 14.8 g. (0.04 mole) of 4-iodobutyltrimethylammonium iodide in a mixture of 100 ml. of absolute ethanol and 120 ml. of ethyl acetate was heated under reflux overnight and then cooled. The crystalline precipitate which appeared was collected on a filter, washed with ethyl acetate and recrystallized from ethanol–ethyl acetate.

Pentamethylene Bis-(conidinium Iodide), Hexamethylene Bis-(conidinium Bromide) and Decamethylene Bis-(conidinium Bromide) (Table V).—These bis-quaternary salts of conidine were prepared by treating at room temperature a freshly distilled sample of conidine with one-half mole of the appropriate dihalide using ether or acetone as solvent. The products crystallized from the reaction mixtures and were collected by filtration after standing 24 hours. They were recrystallized from acetone. All three compounds were very hygroscopic.

INDIANAPOLIS, IND.

(37) (a) W. Marckwald, *Ber.*, **29**, 43 (1896); (b) A. Lipp, *Ann.*, **289**, 173 (1895).

(38) The procedure is essentially that used by A. P. Gray, D. C. Schlieper, E. E. Spinner and C. J. Cavallito, THIS JOURNAL, **77**, 3648 (1955), for preparing 3-bromopropyltrimethylammonium bromide.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA]

d- and *l*-Polyconidine

BY MADELINE S. TOY[1] AND CHARLES C. PRICE

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2-(β-Hydroxyethyl)-piperidine has been resolved through recrystallization of the *d*-10-camphorsulfonate. By conversion to the β-chloroethyl compound and alkaline cyclization, *d*- and *l*-conidine were obtained. Polymerization with boron fluoride-etherate catalysis produced optically active, crystalline, isotactic *d*- and *l*-polyconidine, m.p. 94°, $[\alpha]_D \pm 140°$.

Earlier efforts to prepare crystalline isotactic polyamines from propyleneimines[2] were disappointing in that conditions for obtaining polymers of high molecular weight were not available. We were therefore stimulated by the discovery that conidine could be polymerized to high molecular weight polymers[3] to investigate the preparation of this polymer in optically active, isotactic form. In addition to the interest in the difference in physical properties due to configurational changes at the asymmetric centers in each monomer unit, the preparation of optically active polymers with functional groups capable of catalytic activity might produce synthetic compounds analogous to the optically active protein catalyst systems.

For this purpose, we have resolved *dl*-2-(β-hydroxyethyl)-piperidine (I)[3] by careful recrystallization of the *d*-10-camphorsulfonate salt (II) from ethanol–ether. Since there was a strong tendency for the racemic salt (m.p. 124°) to separate, rather than the diastereoisomeric forms (m.p. 168 and 142°), the conditions for resolution are critical. A great deal of the active material was obtained by very slow crystallization so as to obtain large enough crystals of the diastereoisomeric salts to make hand separation effective.

Conversion of the alcohol to the chloride III[3] proceeded in much better yield when the amine was converted to the hydrochloride before addition of thionyl chloride.

When *d*-conidine (IV) was polymerized by bubbling gaseous boron fluoride into it, it was rapidly converted to a white polymeric powder. This low molecular weight benzene-soluble polymer, m.p. 75°, $[\alpha]_D$ +12.7°, proved to contain one boron fluoride molecule for each amine unit.

By use of boron fluoride-etherate catalyst in an ether solution of monomer, excellent conversion to moderately high molecular weight polymer was achieved within a week or two at room temperature. This polymer, with a strong optical rotation of opposite sign to that of the monomer from which it was formed, gave a sharply crystalline X-ray pattern. The principal diffraction bands are summarized in Table I.

Since *d*- or *l*-poly-(propylene oxide) chains are evidently interchangeable in the crystal lattice, as indicated by the identical X-ray patterns and melting points for *d*-polymer, *l*-polymer and mixtures of the two, it seemed of interest to examine mixtures of *d*- and *l*-polyconidine. Equal amounts of the two were dissolved in benzene and the solution was freeze-dried. The racemic isotactic polymer so produced had the same melting point but,

(1) This work was supported by a grant from the California Research Corporation.

(2) Y. Minoura, M. Takebayashi and C. C. Price, THIS JOURNAL, **81**, 4689 (1959).

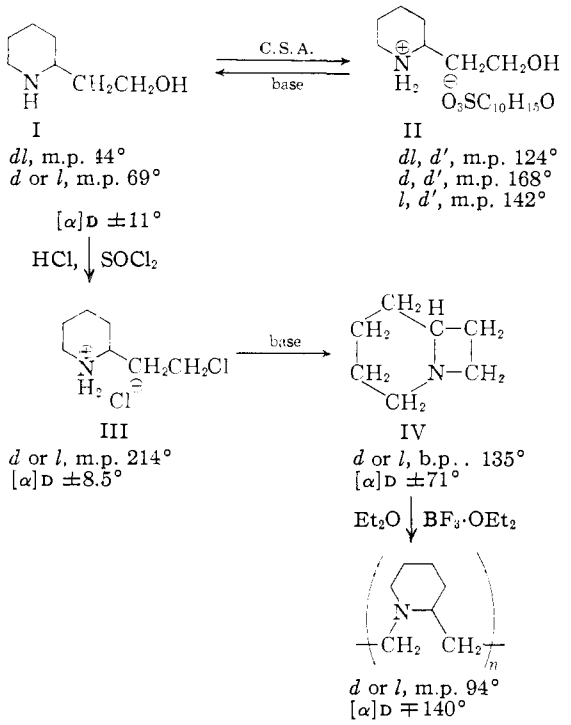
(3) E. R. Lavagnino and E. C. Kornfeld, private communication; E. R. Lavagnino, R. R. Chauvette, W. N. Cannon and E. C. Kornfeld, THIS JOURNAL, **82**, 2609 (1960).

TABLE I

INTERPLANAR SPACINGS AND INTENSITIES FROM X-RAY DIAGRAMS OF POLY-*d*-CONIDINE AND RACEMIC ISOTACTIC POLYCONIDINE

Poly-*d*-conidine		Racemic isotactic polyconidine	
Spacings, Å.	Intensities	Spacings, Å.	Intensities
6.27	Very strong	9.93	Strong
5.53	Very, very strong	5.57	Very strong
5.03	Very, very strong	4.98	Very, very strong
4.64	Very, very weak	4.75	Medium weak
4.37	Medium	4.13	Medium strong
4.13	Medium weak	2.82	Medium
3.30	Medium	2.43	Very, very weak
2.95	Weak	2.29	Weak
2.85	Very weak	2.07	Weak
		1.92	Very weak

as shown in Table I, a markedly different X-ray diffraction pattern. It is perhaps not surprising that the larger, bulkier group attached to the polymer backbone in polyconidine would not permit the mixed crystal formation which occurs for poly(propylene oxide). The data suggest rather that racemic compound formation has occurred.



Experimental

dl-2-(β-**Hydroxyethyl**)-**piperidine**, obtained through the courtesy of Dr. E. C. Kornfield, Eli Lilly and Co., Indianapolis 6, Ind., melted between 35–40°. **The phenylthiourea** derivative was prepared for identification purposes, m.p. 128–129°. *Anal.* Calcd. for $C_{14}H_{20}N_2OS$: C, 63.60; H, 7.63; N, 10.62; S, 12.12. Found: C, 63.43; H, 7.76; N, 10.52; S, 12.12.

dl-2-(β-**Hydroxyethyl**)-**piperidine** *d*-**10-Camphorsulfonate.**—A solution of 35.5 g. (0.275 mole) of *dl*-2-(β-hydroxyethyl)-piperidine in 50 ml. of absolute ethanol was added slowly with stirring to a solution of 64.0 g. (0.275 mole) of commercial *d*-10-camphorsulfonic acid in 80 ml. of absolute ethanol maintained between 0–10° with an ice-bath. The ice-bath was removed after addition and the mixture was kept at room temperature overnight. Absolute ethanol (25 ml.) was then recovered by distillation. The residue was cooled and anhydrous ether was added. The crude *dl*-2-(β-hydroxyethyl)-piperidine *d*-10-camphorsulfonate was collected and dried; yield 69.0 g., m.p. 118–128°.

Two additional fractions, 3.5 g. (m.p. 85–98°) and 6.5 g. (m.p. 110–120°), of the crude product were recovered from the mother liquor by increasing the amount of ether added. The filtrate was evaporated on a steam-bath and the oily residue failed to crystallize. The total yield was 79.0 g. (79.4%).

1. **Fractional Crystallization of Crude** *dl*-2-(β-**Hydroxyethyl**)-**piperidine d-10-Camphorsulfonate.**—Crude *dl*-2-(β-hydroxyethyl)-piperidine *d*-10-camphorsulfonate (m.p. 118–128°), 69.0 g., was dissolved in 70 ml. of absolute ethanol at 60–70°, filtered and kept at room temperature overnight. The white crystalline solid was filtered and dried; yield 12.2 g., m.p. 145–155°, as fraction I.

The filtrate of fraction I was cooled in a refrigerator for 30 minutes and was then kept at room temperature for 3 hours. The solid was filtered and dried; yield 1.5 g., m.p. 140–145°, as fraction II.

The filtrate of fraction II was cooled in a refrigerator for 10 minutes and was then kept at room temperature for 18 hours. The solid was filtered and dried; yield 5.6 g., m.p. 122–125°, as fraction III.

The filtrate of fraction III was cooled in a refrigerator for 20 minutes. The solid was filtered and dried; yield 10.5 g., m.p. 122–127°, as fraction IV.

The filtrate of fraction IV was cooled overnight in a refrigerator. The solid was filtered and dried; yield 5.4 g., m.p. 120–125°, as fraction V.

Anhydrous ether was added to the filtrate of fraction V. The solid was filtered and dried; yield 20.1 g., m.p. 119–122°, as fraction VI.

An additional amount of anhydrous ether was added to the filtrate of fraction VI and it was cooled overnight. The solid was filtered and dried; yield 1.5 g., m.p. 122–124°, as fraction VII.

Excess ether was added to the filtrate of fraction VII and it was cooled for days. The solid was filtered and dried; yield 0.5 g., m.p. 118–124°, as fraction VIII.

The filtrate of fraction VIII was evaporated on a steam-bath. The residue remaining was negligible.

d-2-(β-**Hydroxyethyl**)-**piperidine** *d*-**10-Camphorsulfonate** (*d,d'*-**Salt**).—Fraction I (m.p. 145–155°, 12.2 g.) and fraction II (m.p. 140–145°, 1.5 g.) were combined and dissolved in 25–35 ml. of absolute ethanol at 60–70°. After cooling to room temperature, ether was added. The white crystalline solid was recrystallized from absolute ethanol and ether or acetone and dried; yield 9.0 g. (9.0%) of crystalline *d*-2-(β-hydroxyethyl)-piperidine *d*-10-camphorsulfonate (*d,d'*-salt), m.p. 168°, [α]D +32.4° (2%, $CHCl_3$).

Anal. Calcd. for $C_{17}H_{31}SO_5N$: C, 56.48; H, 8.64; N, 3.87; S, 8.87. Found: C, 56.37; H, 8.83; N, 4.00; S, 9.17.

The filtrate of the product was cooled. The solid was filtered and dried; yield 0.6 g., m.p. 164–166°. This filtrate was concentrated and ether added. The solid was filtered and dried; yield 2.5 g., m.p. 118–123°. This filtrate was evaporated and no residue was obtained.

dl-2-(β-**Hydroxyethyl**)-**piperidine** *d*-**10-Camphorsulfonate** (*dl,d'*-**Salt**).—Fraction III (m.p. 122–125°, 5.6 g.), fraction IV (m.p. 122–127°, 10.5 g.) and fraction V (m.p. 120–125°, 5.4 g.) were combined and dissolved in 35 ml. of absolute ethanol at 60–70°. The liquid was cooled to room temperature and ether was added. The solid was recrystallized from absolute ethanol and ether; yield 13.4 g. of crystalline *dl*-2-(β-hydroxyethyl)-piperidine *d*-10-camphorsulfonate (*dl, d'*-salt), m.p. 123–124°, [α]D +29.0° (2%, $CHCl_3$).

Anal. Calcd. for $C_{17}H_{31}SO_5N$: C, 56.48; H, 8.64; N, 3.87; S, 8.87. Found: C, 56.58; H, 8.71; N, 3.70; S, 8.74.

The filtrate was evaporated on a steam-bath until slight precipitation appeared around the flask. Ether was added and stirred. The solid was filtered and dried; yield 6.5 g., m.p. 118–122°. Evaporation of this filtrate left no residue.

Fraction VI (m.p. 119–122°, 20.1 g.), fraction VII (m.p. 122–124°, 1.5 g.), fraction VIII (m.p. 118–124°, 0.5 g.), and other fractions melting around 120° (19.0 g.), were combined and repeatedly recrystallized from boiling acetone and ether and dried; yield 32.4 g., m.p. 123–124° of *dl-d'* salt. The total yield was 45.8 g. (46.0%).

The filtrate was evaporated on a steam-bath. The oily residue failed to crystallize.

Resolution by Fractional Reaction with the Resolving Agent.—A solution of 57.0 g. (0.246 mole) of commercial *d*-10-camphorsulfonic acid in 80 ml. of absolute ethanol was added slowly to a solution of 40.7 g. (0.316 mole) of *dl*-2-(β-hydroxyethyl)-piperidine in 100 ml. of absolute ethanol at 0–10° with stirring. The reaction mixture was evacuated on a steam-bath under reduced pressure. The distillate, 80 ml., was basic. The residual liquid was seeded with *d*-*d'* salt (m.p. 167–168°) and kept at room temperature overnight. The solid was filtered and dried; yield 21.8 g., m.p. 149–156°, which, after repeated recrystallizations from absolute ethanol and ether, yielded 16.6 g. (17.0%) of *d*,*d'*-salt, m.p. 166–168°.

Solid (m.p. 118–131°, 54.3 g.) was recovered from the mother liquor by concentration and addition of ether. The oily residue failed to crystallize.

Racemic 2-(β-Hydroxyethyl)-piperidine.—2-(β-Hydroxyethyl)-piperidine *d*-10-camphorsulfonate (m.p. 128–131°, 54.3 g.) was hydrolyzed by refluxing for 15 minutes with 2.5 moles of 10% aqueous potassium hydroxide. After addition of 69.0 g. of anhydrous potassium carbonate, the two layers which formed were separated. Both layers were extracted with ether. The white needles were discarded and all the ether extracts were combined and dried overnight with anhydrous magnesium sulfate. Ether was recovered from the liquid by distillation. The residue liquid was chilled in a Dry Ice and acetone bath to a transparent solid, which turned to a white solid by scratching while warming the solid to room temperature. The solid was dried over anhydrous calcium chloride; yield 10.0 g. (51.5%) of racemic 2-(β-hydroxyethyl)-piperidine, m.p. 43–44°, $[\alpha]_D$ zero (3%, $CHCl_3$).

Anal. Calcd. for $C_7H_{15}NO \cdot {}^1/_8H_2O$: C, 64.00; H, 11.62; N, 10.61. Found: C, 64.00; H, 11.56; N, 10.54.

Repeated Fractional Reaction with the Resolving Agent.—A solution of 12.6 g. (0.0543 mole) of commercial *d*-10-camphorsulfonic acid in 20 ml. of absolute ethanol was added slowly to a solution of 14.0 g. of racemic 2-β-(hydroxyethyl)-piperidine (m.p. 43–44°) in 43 ml. of absolute ethanol at 0° with stirring. Anhydrous ether was added to the reaction mixture and it was cooled in a refrigerator overnight. The solid was filtered and dried; yield 9.8 g., m.p. 125–130°. The filtrate was concentrated until the distillate turned basic and ether was added. The solid was washed with ether and dried; yield 8.2 g., m.p. 125–130°. The filtrate and ether washing were combined and dried with anhydrous magnesium sulfate. The liquid was distilled on a steam-bath until the distillate turned basic. The residual liquid was chilled in a Dry Ice and acetone bath to yield a transparent solid, which turned to a white solid by scratching while warming the solid to room temperature. The solid was dried over anhydrous calcium chloride; yield 5.7 g., m.p. 41–50°, $[\alpha]_D$ −1.4° (4%, $CHCl_3$).

Resolution by Segregation of Diastereoisomeric Derivative by Crystallization.—A solution of 147.5 g. (0.635 mole) of commercial *d*-10-camphorsulfonic acid in 170 ml. of absolute ethanol was added dropwise to a solution of 164 g. (1.271 moles) of 2-(β-hydroxyethyl)-piperidine in 320 ml. of absolute ethanol at 0–10° with stirring. The reaction mixture was cooled in a refrigerator overnight. A few large lath-like crystals (*d*,*d'*-salt) were observed. After cooling for several days, smaller crystals of similar shape were formed. The crystals were collected and washed with 100 ml. of anhydrous ether; yield 63.2 g., m.p. 164–167°.

Ether (120 ml.) was added to the mother liquor and it was cooled for several days. The solid was collected and dried; yield 22.1 g., m.p. 158–164°.

Ether (210 ml.) was added to the filtrate and it was cooled overnight. Large crystals of mixed shapes were observed. The lath-like crystals melted at 167–169° and the thick prismatic crystals (*l*,*d'*-salt) melted at 141–143°. The two types of crystals were separated mechanically. Slow crystallization, which varied from one day to months, from a very dilute solution of mixed solvent of acetone, ethanol and ether, afforded a racemic crystal mixture or a conglomerate of sufficiently large crystals to permit their segregation by hand picking. These conditions were hard to control. Partial crystallization of one component alone was sometimes induced by inoculating the supersaturated solution with a crystal of one form or the other, although only rarely did uniform deposits of one variety occur.

Isolation of *l*,*d'*-Salt.—Mechanically separated crystals of *l*,*d'*-salt (m.p. 141–143°), 3.0 g., were recrystallized twice from acetone. The tiny tabular crystals were filtered and dried; yield 1.3 g. (43.3%), m.p. 141–142°, $[\alpha]_D$ +23.6° (2% $CHCl_3$).

Anal. Calcd. for $C_{17}H_{31}SO_5N$: C, 56.48; H, 8.64; N, 3.87; S, 8.87. Found: C, 56.43; H, 8.61; N, 3.94; S, 8.87.

Hydrolysis of *l*,*d'*-Salt.—*l*-2-(β-Hydroxyethyl)-piperidine *d*-10-camphorsulfonate (m.p. 141–142°, 19.5 g.) was hydrolyzed by refluxing for 15 minutes with 2.5 moles of 10% aqueous potassium hydroxide. After addition of 25.0 g. of anhydrous potassium carbonate, two layers were formed, but not separated. The top layer disappeared, after continuous ether extraction of both layers had been carried out for two hours. The aqueous layer was separated and extracted with ether twice. The white crystals and aqueous layer were then discarded and the ether extracts were combined with the top ether layer from continuous ether extraction. The ether layer was dried with anhydrous magnesium sulfate and distilled on the steam-bath until the distillate turned basic. The residual liquid solidified at room temperature and the solid was recrystallized from anhydrous ether and dried; yield 3.5 g. (50.4%) of *l*-2-(β-hydroxyethyl)-piperidine, m.p. 69–70°, $[\alpha]_D$ −11.0° (3% $CHCl_3$).

Anal. Calcd. for $C_7H_{15}NO$: C, 65.11; H, 11.63; N, 10.86. Found: C, 65.33; H, 11.66; N, 10.78.

Hydrolysis of *d*,*d'*-Salt.—The same alkaline hydrolysis was carried out on 29.2 g. of *d*-2-(β-hydroxyethyl)-piperidine *d*-10-camphorsulfonate (m.p. 168°); yield 5.6 g. (53.8%) of *d*-2-(β-hydroxyethyl)-piperidine, m.p. 68–69°, $[\alpha]_D$ +11.0° (3%, $CHCl_3$).

Anal. Calcd. for $C_7H_{15}NO$: C, 65.11; H, 11.63; N, 10.86. Found: C, 65.09; H, 11.63; N, 10.84.

***d*-2-(β-Chloroethyl)-piperidine Hydrochloride.**—Anhydrous hydrogen chloride was bubbled through a solution of 15.9 g. (0.123 mole) of *d*-2-(β-hydroxyethyl)-piperidine (m.p. 68–69°) in 35 ml. of anhydrous chloroform at 0–10° for less than a half-hour; white solid appeared but was not isolated. Anhydrous chloroform, 70 ml., was added and bubbling of anhydrous hydrogen chloride was continued until saturation. This saturated solution was added dropwise with stirring to 60 g. (0.504 mole) of thionyl chloride maintained at 0–10°. This solution was stirred at room temperature for one hour and the temperature was increased slowly to refluxing for another hour. Absolute ethanol (45.0 ml.) was added slowly to the cooled solution and then it was refluxed for another hour with stirring. Upon cooling, white needles appeared. After keeping at room temperature overnight, the white needles were filtered, washed with a small amount of cold ethanol and anhydrous ether and dried; yield 16.7 g., m.p. 213–214°.

An additional quantity of the product was recovered from the mother liquor and recrystallized from ethanol, acetone and ether and dried; yield 4.7 g., m.p. 213–214°. The total yield of *d*-2-(β-chloroethyl)-piperidine hydrochloride was 21.4 g. (94.7%), m.p. 213–214°, $[\alpha]_D$ +8.76° (2% $CHCl_3$).

Anal. Calcd. for $C_7H_{14}NCl \cdot HCl$: C, 45.70; H, 8.15; N, 7.60; Cl, 38.59. Found: C, 45.89; H, 8.00; N, 7.83; Cl, 38.55.

***l*-2-(β-Chloroethyl)-piperidine Hydrochloride.**—The above procedure was carried out for 22.3 g. of *l*-2-(β-hydroxyethyl)-piperidine (m.p. 69–70°); yield 17.9 g. (56.3%) of *l*-2-(β-chloroethyl)-piperidine hydrochloride, m.p. 211–213°. A sample used for analytical purposes was recrystallized from acetone and ethanol; m.p. 214–215°, $[\alpha]_D$ −8.40° (1%, $CHCl_3$).

Anal. Calcd. for $C_7H_{14}NCl \cdot HCl$: C, 45.70; H, 8.15; N, 7.60; Cl, 38.59. Found: C, 45.45; H, 8.16; N, 7.59; Cl, 38.33.

***d*-Conidine.**—The procedure used on 20.8 g. of *d*-2-(β-chloroethyl)-piperidine hydrochloride (m.p. 213–214°) was that of Lavagnino[3]; yield 3.99 g. (31.9%) of colorless *d*-conidine, b.p. 134–136°, $[\alpha]_D$ +71.7° (3.7%, $CHCl_3$).

Anal. Calcd. for $C_7H_{13}N$: C, 75.67; H, 11.71; N, 12.61. Found: C, 75.73; H, 11.81; N, 12.47.

***l*-Conidine.**—The same procedure was carried out on 17.0 g. of colorless *l*-2-(β-chloroethyl)-piperidine hydrochloride

(m.p. 211–213°); yield 5.42 g. (53%), b.p. 130–132°, $[\alpha]_D$ −71.0° (4.8%, $CHCl_3$).

Anal. Calcd. for $C_7H_{13}N$: N, 12.61. Found: N, 12.52.

Poly-*d*-conidine Boron Fluoride.—*d*-Conidine (b.p. 134–136°, *ca.* 1 g.) was added to a nitrogen-filled Carius tube. After boron fluoride had been bubbled through for 1.5 minutes, the liquid turned to yellow solid. After standing at room temperature for 5 days, the polymer was dissolved in 20 ml. of benzene, washed three times with 10% sodium hydroxide, and then with water, until the washing became neutral. The benzene layer was dried with anhydrous potassium carbonate and freeze-dried; yield, 1.0 g. of almost white poly-*d*-conidine boron fluoride, m.p. 73–75°, $[\alpha]_D$ +12.7° (1.5% $CHCl_3$), $[\eta]$ 0.047 in benzene at 26°, molecular weight 4300 (Rast).

Anal. Calcd. for $(C_7H_{13}N\cdot BF_3)_n$: C, 46.98; H, 7.27; N, 7.83. Found: C, 47.52; H, 7.44; N, 7.77.

Poly-*d*-conidine boron fluoride was soluble in benzene and chloroform and insoluble in ether, acetone and water at room temperature. It was soluble in boiling acetone and boiling water.

Poly-*d*-conidine.—*d*-Conidine (b.p. 134–136°, *ca.* 2 ml.) was added to a nitrogen-filled Carius tube and one to two drops of redistilled boron fluoride etherate was added. It was then sealed and kept at room temperature for five days. The white polymer was dissolved in 240 ml. of boiling benzene, cooled to room temperature, washed three times with 250-ml. portions of 10% aqueous sodium hydroxide, and then washed with water until the washings became neutral. The benzene layer was freeze-dried to yield 1.7 g. of white isotactic poly-*d*-conidine, m.p. 92–94°, $[\alpha]_D$ −140.8° (1.4%, $CHCl_3$), $[\eta]$ 0.33 in benzene at 26°.

Anal. Calcd. for $(C_7H_{13}N)_n$: C, 75.67; H, 11.71; N, 12.61. Found: C, 75.52; H, 11.76; N, 12.60.

Poly-*d*-conidine was highly crystalline by X-ray powder diagram (Table I). It was soluble in benzene, chloroform and carbon tetrachloride and fairly soluble in ethanol, boiling water and boiling pyridine, but it was insoluble in acetone and ether at boiling or room temperature.

Poly-*l*-conidine.—The above procedure was carried out on 2.81 g. of *l*-conidine (b.p. 130–132°), except the sealed tube was kept at room temperature for 14 days instead of 5 days; yield 2.56 g. (90.0%) of white isotactic poly-*l*-conidine, m.p. 92–94°, $[\alpha]_D$ +140.8° (1.4%, $CHCl_3$), $[\eta]$ 0.45 in chloroform at 25.0°.

Anal. Calcd. for $(C_7H_{13}N)_n$: C, 75.67; H, 11.71; N, 12.61. Found: C, 75.54; H, 11.54; N, 12.62.

Poly-*l*-conidine was soluble in benzene and chloroform and insoluble in water, pyridine, acetone, ether, N,N-dimethylformamide, nitromethane and nitrobenzene at room temperature. It was slightly soluble at boiling temperature in several solvents: water, pyridine, ethanol, N,N-dimethylformamide and nitrobenzene.

Racemic Isotactic Polyconidine.—Isotactic poly-*d*- and *l*-conidine (each m.p. 92–94°, 0.0756 g.) were mixed and dissolved in 35.0 ml. of warm benzene and freeze-dried; yield 0.12 g. of racemic isotactic polyconidine, m.p. 91–93°, $[\alpha]_D$ 0.00 (1%, chloroform).

Racemic isotactic polyconidine was highly crystalline. The calculated interplanar spacings (Å.) and intensities are cited in Table I.

Racemic Atactic Polyconidine.—When the above polymerization procedure was carried out on 2.0 ml. of *dl*-conidine, only yellow, translucent, tacky and soft polymer was formed.

PHILADELPHIA 4, PENNA.

[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Veratrum Alkaloids. XLII.[1] The Structures of Desacetylprotoveratrine A and Desacetylprotoveratrine B[2]

BY S. MORRIS KUPCHAN, C. IAN AYRES AND RUPRECHT H. HENSLER

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The structures of desacetylprotoveratrine A and desacetylprotoveratrine B have been elucidated. Desacetylprotoveratrine A is protoverine 3-(*d*)-2′-hydroxy-2′-methylbutyrate 6-acetate 15-(*l*)-2′-methylbutyrate (VIII). Desacetylprotoveratrine B is protoverine 3-(*d*)-*threo*-2′,3′-dihydroxy-2′-methylbutyrate 6-acetate 15-(*l*)-2′-methylbutyrate (XII).

Desacetylprotoveratrine A[3] and desacetylprotoveratrine B ("desacetylneoprotoveratrine")[4,5] are hypotensive triester constituents of alkaloidal extracts of veratrum species. Desacetylprotoveratrine A may be obtained by methanolysis[3] of the hypotensive tetraester protoveratrine A (VII)[6] and desacetylprotoveratrine B may be obtained by methanolysis[4] of protoveratrine B (IX).[6] Nevertheless, the isolation of the triesters from extracts made under mild conditions known to leave intact sensitive germine triesters such as germitrine and neogermitrine[5] would suggest that the desacetylprotoveratrines may be of primary origin in the plant.

Our interest in the desacetylprotoveratrines arose from a study of the mild mineral acid hydrolysis of protoveratrine A and protoveratrine B. It was shown that, in each case, an acetyl grouping could be selectively removed to yield the corresponding naturally occurring triester. Due to the closely related structures of the protoveratrines, it seemed reasonable to assume, as a working hypothesis, that the acid-labile acetyl grouping was attached to the same position in the nucleus, *i.e.*, either C_6 or C_7. A strong indication that the C_7-acetate was acid-labile came from the following sequence. Protoveratrine A 16-isobutyrate[6] (I) on acid hydrolysis afforded a desacetylprotoveratrine A 16-isobutyrate (II). The latter compound on chromic acid oxidation yielded dehydrodesacetylprotoveratrine A 16-isobutyrate (III). The rotatory dispersion curve of III was virtually superimposable upon that of 7-dehydroprotoverine 3,6,15,16-tetraacetate (VI) (Fig. 1).[7] The structure of VI was unequivocally determined by synthesis. Protoverine 3,6,16-triacetate (IV)[8] (so-

(1) Part XLI in the series: S. M. Kupchan and N. Gruenfeld, *J. Am. Pharm. Assoc., Sci. Ed.*, **48**, 737 (1959).

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