When base 1 was dissolved in dimethyl sulfoxide-d_6 and a solution of deuterium chloride in deuterium oxide added, the resulting salt solution displayed signals for the individual aromatic protons at τ 3.28, 3.16, and 2.98. After the mixture had been heated for 24 hr at 100° only the aromatic proton signal at τ 3.28 had disappeared.

The **hydrobromide** crystallized from methanol as colorless needles: mp 258–260° dec; $\lambda_{max}^{95\% EtOH}$ 224 mμ sh (log ε 3.91), 273 sh (3.34), 282 (3.53), 288 sh (3.51), 290 sh (3.42).

Anal. Calcd for $C_{21}H_{28}BrNO_5$: C, 55.78; H, 5.79; N, 3.09; OCH_3, 27.50. Found: C, 55.66; H, 5.80; N, 3.03; OCH_3, 27.41.

Comparison of 11-Hydroxy-2,3,9,10-tetramethoxy-5,6,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizine (1) with Stepharotine.—About 1 mg of stepharotine hydrobromide was dissolved in water and the base liberated by addition of ammonia solution. The mixture was evaporated to dryness under reduced pressure. The residue was extracted with methylene chloride, filtered, and concentrated under reduced pressure, and the residue taken up in carbon tetrachloride.

The infrared spectrum of the resulting solution was determined using a 2-μl microcell with a Perkin-Elmer Model 21 spectrophotometer. Our hydroxy base (1) measured in the same way showed significant differences, particularly in the 8–11-μ region. Similar differences were reported to us by Dr. Kozuka who kindly compared our hydroxy base (1) with stepharotine, using chloroform as the solvent and making the infrared measurements with a Hitachi instrument.

2,3,9,10,11-Pentamethoxy-5,6,13,13a-tetrahydro-8H-dibenzo-[a,g]quinolizine (2).—To a solution of 300 mg of hydroxy base 1 in 50 ml of acetone, 1.6 g (excess) of diazomethane in 150 ml of ether was added followed by 20 ml of methanol. After 12 hr at 0° the mixture was allowed to stand 48 hr at room temperature before removal of the solvents and excess diazomethane under reduced pressure. The residue was dissolved in 50 ml of methylene chloride, then chromatographed on neutral alumina (8 × 1 cm column), and eluted with 75 ml of the same solvent. The yellow oil obtained by evaporation was crystallized from methylene chloride–ether affording 200 mg (64%) of almost colorless rectangular needles, mp 138–140° (lit.[3] mp 148–149°). In our hands a sample of the pentamethoxy compound (2) prepared by a method essentially that of Tomita, *et al.*, also melted at 138–140°. Samples of 2 prepared by the methylation of the hydroxy base and by the method of Tomita, *et al.*,[3] were found identical by means of infrared spectra and the mixture melting point: $\lambda_{max}^{75\% EtOH}$ 224 sh (log ε 3.97), 275 sh (3.34), 283 (3.48), 286 sh (3.44), 293 sh (3.30); nmr ($CDCl_3$) τ 6.20, 6.14, 6.10 (each s, 3, CH_3), 6.16 (s, 6, two CH_3), 3.52, 3.39, 3.26 (each s, 1, aromatic H).

Anal. Calcd for $C_{22}H_{27}NO_5$: C, 68.55; H, 7.06; N, 3.63. Found: C, 68.47; H, 7.11; N, 3.62.

Registry No.—**1**, 19598-17-5; **1** HBr, 19598-18-6; **2**, 7668-86-2; **5**, 19587-70-3; **8**, 19587-71-4; **9**, 19587-72-5; **10**, 19587-73-6; **12**, 19613-63-9; **13**, 19587-74-7; **14**, 19587-75-8; **15**, 19587-76-9.

Acknowledgment.—The authors wish to acknowledge the gracious cooperation of Drs. M. Tomita and M. Kozuka in providing us with a sample of stepharotine and of the synthetic[2] pentamethoxy compound 2 as well as numerous nmr and infrared spectra. We are also indebted to Mr. Ernest C. Sunas of the Liggett and Myers Research Laboratories for a spectrometric comparison of our hydroxy base with stepharotine and to Dr. Charles G. Moreland of North Carolina State University for some 100-Mc nmr measurements.

The Resolution and Absolute Configuration of the Racemic Isomer of Anaferine

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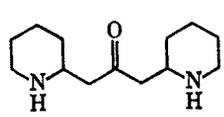
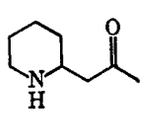
The absolute configuration of the isomers of the alkaloid anaferine, 1,3-bis(2-piperidyl)-2-propanone, was established by ORD analysis of the hydrochloride and the base obtained from the resolved dimandelates and of the isomers of pipecolic acid derived from the hydrochlorides. L-(+)-1,3-bis(2-piperidyl)-2-propanone is (*S,S*)-(+)-1,3-bis(2-piperidyl)-2-propanone and D-(−)-1,3-bis(2-piperidyl)-2-propanone is (*R,R*)-(−)-1,3-bis-(2-piperidyl)-2-propanone.

Anaferine (1) [1,3-bis(2-piperidyl)-2-propanone] was reported for the first time as a naturally occurring compound by Rother, *et al.*, in 1962.[1] This compound was originally obtained by Anet, *et al.*,[2] in their attempted synthesis of sparteine by condensation of 5-aminopentanal with acetonedicarboxylic acid at pH 11. It has also been synthesized by Schöpf, *et al.*,[3] by condensation of Δ^1-piperideine and acetonedicarboxylic acid at pH 11.5. Later it was prepared in this laboratory[4] in admixture with hygrine, cuscohygrine, anahygrine, and isopelletierine (2) from Δ^1-piperideine, 2-hydroxy-1-methylpyrrolidine, and acetonedicarboxylic acid at pH 12.

Three stereoisomers are possible: (+)-, (−)-, and *meso*-1,3-(2-piperidyl)-2-propanones. Schöpf, *et al.*,[3] separated *meso*- and DL-1,3-bis(2-piperidyl)-2-propanones as the hydrobromides and picrates. Anaferine isolated from *Withania somnifera* corresponds to the *meso* isomer.[5]



1



2

We have separated *meso*-1,3-bis(2-piperidyl)-2-propanone as the L-(+)- and D-(−)-dimandelate, (+)-1,3-bis(2-piperidyl)-2-propanone as the L-(+)-dimandelate, and (−)-1,3-bis(2-piperidyl)-2-propanone as the D-(−)-dimandelate. Using L-(+)-mandelic acid to resolve the isomeric mixture, *meso*-1,3-bis(2-piperidyl-2-propanone L-(+)-dimandelate and (+)-1,3-bis(2-piperidyl)-2-propanone L-(+)-dimandelate

(1) A. Rother, J. M. Bobbitt, and A. E. Schwarting, *Chem. Ind.* (London), 654 (1962).

(2) E. F. L. J. Anet, G. K. Hughes, and E. Ritchie, *Aust. J. Sci. Res.*, **3A**, 635 (1950).

(3) C. Schöpf, G. Benz, F. Braun, H. Hinkel, and R. Rokohl, *Angew. Chem*, **65**, 161 (1953).

(4) M. M. El-Olemy, A. E. Schwarting, and W. J. Kelleher, *Lloydia*, **29**, 58 (1966).

(5) A. E. Schwarting, J. M. Bobbitt, A. Rother, C. K. Atal, K. L. Khanna, J. D. Leary, and W. G. Walter, *ibid.*, **26**, 258 (1963).

were obtained sequentially. In the same manner, using D-(−)-mandelic acid, *meso*-1,3-bis(2-piperidyl)-2-propanone D-(−)-dimandelate, and (−)-1,3-bis-(2-piperidyl)-2-propanone D-(−)-dimandelate were obtained. Each of the dimandelate salts was converted into the corresponding dihydrochloride and dipicrate.

(+)-1,3-Bis(2-piperidyl)-2-propanone dihydrochloride yielded L-(−)-pipecolic acid and (−)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride yielded D-(+)-pipecolic acid on chromic acid oxidation. (+)-1,3-Bis(2-piperidyl)-2-propanone thus possesses the L configuration and (−)-1,3-bis (2-piperidyl)-2-propanone the D configuration.

Optical rotatory dispersion curves obtained for (+)- and (−)-1,3-bis(2-piperidyl)-2-propanone dihydrochlorides as well as (+)- and (−)-1,3-bis(2-piperidyl-2-propanone bases, generated from this salt, gave curves (Figure 1) which, when compared with those[6] of (+)- and (−)-isopelletierine sulfates and bases (2), confirm the conclusion that (+)-1,3-bis-(2-piperidyl)-2-propanone possesses the L configuration and (−)-1,3-bis(2-piperidyl)-2-propanone the D configuration.

ORD curves obtained for the pipecolic acid enantiomers obtained from the oxidation of (+)- and (−)-1,3-bis(2-piperidyl)-2-propanone dihydrochlorides corresponded to the curves of reference L-(−)- and D-(+)-pipecolic acids and are similar to those reported by Craig and Roy.[7] These data prove unambiguously that (−)- and (+)-1,3-bis(2-piperidyl)-2-propanones possess the D and L configuration, respectively.

Thus L-(+)-1,3-bis(2-piperidyl)-2-propanone is (*S*,*S*)-(+)-1,3-bis(2-piperidyl)-2-propanone[8] and D-(−)-1,3-bis(2-piperidyl)-2-propanone is (*R*,*R*)-(−)-1,3-bis-(2-piperidyl)-2-propanone.

Experimental Section[9]

Δ^1-Piperideine (≡ α-Tripiperideine) (4).—This compound, prepared according to the procedure of Schöpf, *et. al.*,[10] gave mp 59–60° (lit.[10] mp 61–62°).

Preparation of 1,3-Bis(2-piperidyl)-2-propanone Isomers.—Δ^1-Piperideine (2.28 g) was dissolved in 0.1 *N* sodium hydroxide solution (150 ml). Acetonedicarboxylic acid (2 g) was added and the reaction was conducted as previously described.[4] Analysis by tlc[9] showed the presence of *meso*- and DL-1,3-bis(2-piperidyl)-2-propanone and isopelletierine (2) (R_f 0.68).

The mixture (3 g) was separated by a countercurrent distribution system.[4] The mixture, distributed in the first four tubes,

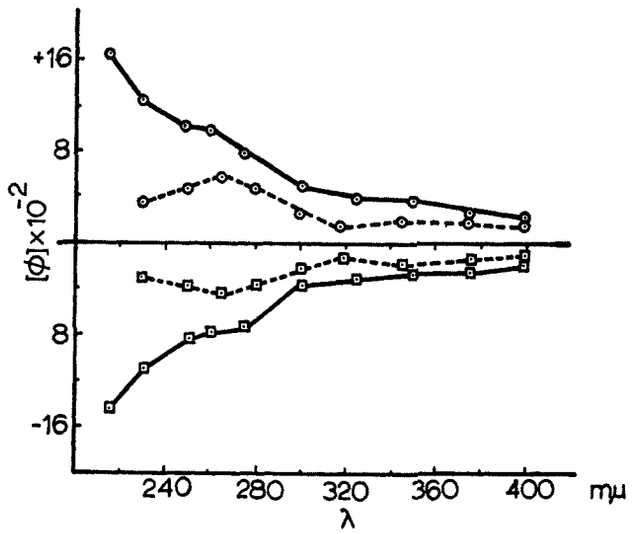


Figure 1.—Optical rotatory dispersion of (+)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride (—⊙—), (+)-1,3-bis(2-piperidyl)-2-propanone (- -⊙- -), (−)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride (—⊡—), and (−)-1,3-bis(2-piperidyl)-2-propanone (- -⊡- -).

was carried through 95 transfers to provide the anaferine isomers (tubes 65–90) and isopelletierine (tubes 50–64).

The hydrochloride was prepared by dissolving the isomeric mixture in anhydrous ether and anhydrous methanol. Dry hydrogen chloride was passed through the solution and the mixture was refrigerated. The crystals were collected by filtration. Analysis by tlc showed the presence of both *meso*- and DL-1,3-bis(2-piperidyl)-2-propanone.[9]

***meso*-1,3-Bis(2-piperidyl)-2-propanone L-(+)-Dimandelate (5).**—A solution of 1,3-bis(2-piperidyl)-2-propanone hydrochloride (3.11 g) in water was basified with sodium hydroxide solution and extracted with chloroform. After drying with anhydrous sodium sulfate, the chloroformic solution was evaporated to dryness *in vacuo* at 40°. The residue, in 40 ml of ethanol, was mixed with L-(+)-mandelic acid (3.16 g) in 10 ml of ethanol. The solution was brought to boiling and passed through a pad of charcoal in a Büchner funnel, then concentrated to 35 ml, and cooled. The crystals (1.6 g) were collected and washed with ethanol. Recrystallization twice from methanol gave 0.7 g of white needles of **5**, mp 169.7–171°, $[\alpha]^{22}D$ +67.4 ± 2° (*c* 0.503, water–methanol, 1:1).

Anal. Calcd for $C_{28}H_{40}N_2O_7$: C, 65.89; H, 7.63; N, 5.30. Found: C, 66.01; H, 7.79; N, 5.14.

(+)-1,3-Bis(2-piperidyl)-2-propanone L-(+)-Dimandelate (6).—The original mother liquor of *meso*-1,3-bis(2-piperidyl)-2-propanone L-(+)-dimandelate was evaporated to dryness *in vacuo* at 40°. The residue was dissolved in 4 ml of methanol, 60 ml of acetone was added, and the solution was cooled overnight. The crystals (660 mg), washed with methanol–acetone (1:10), were recrystallized twice from methanol–acetone to give 380 mg of **6**, mp 141–142.5°, $[\alpha]^{22}D$ +96.3 ± 2° (*c* 0.456, water–methanol, 1:1).

Anal. Calcd for $C_{28}H_{40}N_2O_7$: C, 65.89; H, 7.63; N, 5.30. Found:[11] C, 65.98; H, 7.51; N, 5.34.

An additional amount of **6** was obtained by resolving a sample of DL-1,3-bis(2-piperidyl-2-propanone dihydrochloride (0.78 g) with L-(+)-mandelic acid to give 185 mg of the product, mp 141–142.5°, $[\alpha]^{22}D$ +95.5 ± 2° (*c* 0.492, water–methanol, 1:1).

***meso*-1,3-Bis(2-piperidyl-2-propanone D-(−)-Dimandelate (7).**—1,3-Bis(2-piperidyl-2-propanone hydrochloride (2.66 g) was treated as above except for the addition of 2.7 g of D-(−)-mandelic acid. The crystals (1.2 g) were collected and recrystallized twice from methanol to give 400 mg of **7**, mp 169.5–171.5°, $[\alpha]^{22}D$ −66.8 ± 2° (*c* 0.489, water–methanol, 1:1).

(−)-1,3-Bis(2-piperidyl-2-propanone D-(−)-Dimandelate (8).—The original mother liquor from **7** was treated as before to obtain 412 mg of (−)-1,3-bis(2-piperidyl-2-propanone D-(−)-dimandelate which after three recrystallizations from methanol–

(6) H. C. Beyerman, L. Maat, and J. P. Visser, *Rec. Trav. Chim. Pays-Bas*, **86**, 80 (1967).

(7) J. C. Craig and S. K. Roy, *Tetrahedron*, **21**, 391 (1965).

(8) According to the sequence rule developed by Cahn, *et al.* See R. S. Cahn, C. R. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

(9) Microanalysis was done by Ilse Beetz Mikroanalytisches Laboratorium, 8640 Kronach, West Germany. The countercurrent separation was done using a Craig-Post countercurrent apparatus, Model 2B (number of shakings 20, number of transfers 95, and settling times 5 min). All melting points are corrected and were taken on a Thomas–Hoover capillary melting point apparatus, Arthur H. Thomas Co. Mixture melting points were taken with equal amounts of the two compounds in question. Optical rotations were taken with a Rudolph visual polarimeter, Model 80, O. C. Rudolph & Sons, Inc., using a 0.5-dm tube. ORD data were measured on a Rudolph recording spectropolarimeter, Model 260/658/850/810-609, using a 0.1-dm tube. Thin layer chromatography (tlc) was used routinely in monitoring the reactions and in the separation and resolution of the isomers. The system used was aluminum oxide G with freshly prepared benzene–diethylamine–methanol (99:5:1). The Dragendorff reagent was used to develop the chromatograms. *meso*-1,3-bis(2-piperidyl)-2-propanone gives R_f 0.24 and DL-1,3-bis(2-piperidyl)-2-propanone give 0.36.

(10) C. Schöpf, A. Komzak, F. Braun, and E. Jacobi, *Ann.*, **559**, 1 (1948).

(11) Average of duplicate analyses.

acetone gave 260 mg of **8**, mp 142–143°, $[\alpha]^{22}D$ −96.1 ± 2° (*c* 0.489, water–methanol, 1:1).

An additional amount of **8** was obtained by resolving DL-1,3-bis(2-piperidyl-2-propanone dihydrochloride (0.78 g) using D-(−)-mandelic acid to obtain 188 mg of the product, mp 141–142°, $[\alpha]^{22}D$ −95.7 ± 2° (*c* 0.497, water–methanol, 1:1).

(+)-1,3-Bis(2-piperidyl)-2-propanone Dipicrate (9).—Picric acid (63 mg) was added to a solution of (+)-1,3-bis(2-piperidyl-2-propanone L-(+)-dimandelate (53 mg) in water (2 ml). The mixture was brought to boiling with stirring then cooled for 15 min. The mixture was washed by stirring three times, each with 6 ml of water-saturated ether, removing the ether after each addition. The last traces of ether were removed by a current of air and the mixture was brought to boiling and cooled. The crystals (51 mg) were filtered and washed with ethanol and ether. These were dissolved in 1.1 ml of ethanol and held at 35° (slow evaporation permitted) to obtain 36.5 mg of **9**, mp 128.5–129.5°, $[\alpha]^{22}D$ +12.2 ± 2° (*c* 0.493, methanol–acetone, 1:1).

Anal. Calcd for $C_{25}H_{30}N_8O_{15}\cdot H_2O$: N, 16.00. Found: N, 15.97.

(−)-1,3-Bis(2-piperidyl)-2-propanone Dipicrate (10).—(−)-1,3-Bis(2-piperidyl)-2-propanone D-(−)-dimandelate (53 mg) was treated as above to obtain 54 mg of the product which after two recrystallizations from ethanol gave 25 mg of **10**, mp 128.5–129.5°, $[\alpha]^{22}D$ −11.9 ± 2° (*c* 0.556, methanol–acetone, 1:1), mmp 117–123° with **9**.

Anal. Calcd for $C_{25}H_{30}N_8O_{15}\cdot H_2O$: N, 16.00. Found: N, 16.01.

***meso*-1,3-Bis(2-piperidyl)-2-propanone Dipicrate (11). A.**—*meso*-1,3-Bis(2-piperidyl)-2-propanone L-(+)-dimandelate (53 mg) was treated as above to obtain 64.5 mg of the picrate; this product was recrystallized from ethanol to give 52 mg of **11**, mp 191–192° (lit.[3] mp 195°), $[\alpha]^{22}D$ 0.0° (*c* 0.567, methanol–acetone, 1:1).

B.—*meso*-1,3-Bis(2-piperidyl)-2-propanone D-(−)-dimandelate (53 mg) was treated as above to give, after two recrystallizations from ethanol, 36 mg of **11**, mp 192–193.5° (lit.[3] mp 195°), $[\alpha]^{22}D$ 0.0° (*c* 0.76, methanol–acetone, 1:1), mmp 192–193° (undepressed) with **11** obtained by method A.

DL-1,3-Bis(2-piperidyl)-2-propanone, Dipicrate (12).—A mixture of **9** and **10** (8 mg each) was crystallized from ethanol at 35° to yield 10 mg of **12**, mp 177–179° (lit.[3] mp 179°).

(+)-1,3-Bis(2-piperidyl)-2-propanone Dihydrochloride (13).—A solution of **6** (330 mg) in 4.1 ml of 0.667 *N* hydrochloric acid was extracted four times, each with 15 ml of water-saturated ether, and the aqueous solution was evaporated *in vacuo* over P_2O_5. The residue was dissolved in a minimum volume of methanol, two volumes of acetone were added, and the solution was cooled. The crystals were washed with methanol–acetone (1:2) and recrystallized from methanol–acetone to give 75 mg of **13**, mp 242.5–244°, $[\alpha]^{22}D$ +50.7 ± 2° (*c* 0.736, water–methanol, 1:1).

Anal. Calcd for $C_{13}H_{26}N_2OCl_2$: Cl, 23.905. Found: Cl, 23.68.

(−)-1,3-Bis(2-piperidyl)-2-propanone Dihydrochloride (14).—A solution of **8** (344 mg) in 4.1 ml of 0.667 *N* hydrochloric acid was treated as above (to obtain **13**) to give, after two recrystallizations from methanol–acetone, 73 mg of **14**, mp 242.5–243.5°, $[\alpha]^{22}D$ −49.8 ± 2° (*c* 0.529, water–methanol, 1:1), mmp 240.5–241.5° with **13**.

***meso*-1,3-Bis(2-piperidyl)-2-propanone Dihydrochloride (15).**—A solution of 1.631 g of mixed **5** and **7** in 15 ml of 0.667 *N* hydrochloric acid was treated the same as above (to obtain **13**) to yield, after two recrystallizations from boiling methanol, 585 mg of **15**, mp 224–225.5° (lit. mp 224–225°,[4] 222.5–223.5°[5]).

L-(−)-Pipecolic Acid from (+)-1,3-bis(2-piperidyl)-2-propanone Dihydrochloride.—Chromic acid (238 mg) in water (2 ml) was added to a solution of (+)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride (85 mg) in 50% v/v sulfuric acid solution (8 ml). The mixture was allowed to stand for 30 min, refluxed for 3 hr, and cooled. Sulfur dioxide gas was passed through the solution and excess sulfur dioxide was removed by a current of air. Barium carbonate (30 mg) and saturated solution of barium hydroxide (150 ml) were added. The slightly acidic mixture was neutralized with dilute ammonium hydroxide solution and then filtered. The filtrate was evaporated to dryness and the residue was dissolved in 1.5 ml of methanol. This solution was applied as a streak on a Whatman No. 2 filter paper strip (58 × 25 cm); this was developed with 1-butanol–acetic acid–water (6:1:2). After development to 45 cm, the paper was dried and test strips were sprayed with ninhydrin reagent[12] and developed at 110° for 10 min. The chromatogram was reconstructed and the pipecolic acid area (R_f 0.34) was cut and extracted with ethanol by elution chromatography. The eluate was evaporated to dryness, the residue was dissolved in 0.5 ml of methanol, acetone was added to incipient turbidity (*ca.* 3 ml), and the mixture was cooled. The pipecolic acid obtained (7 mg) was crystallized from methanol–acetone to give 4.5 mg of (−)-pipecolic acid, mp 270–272° dec, $[\alpha]^{22}D$ −26.3 ± 2° (*c* 0.323, water) {lit.[13] mp 268°, $[\alpha]^{24}D$ −26 (*c* 0.43, water)}, mmp 270–272° with reference L-(−)-pipecolic acid (mp 272–274°), mmp 252–257° with reference D-(+)-pipecolic acid (mp 272–274°).

D-(+)-Pipecolic Acid from (−)-1,3-Bis(2-piperidyl)-2-propanone Dihydrochloride.—(−)-1,3-Bis(2-piperidyl)-2-propanone dihydrochloride (76 mg) was oxidized as above. The pipecolic acid isolated (6.5 mg) was crystallized from methanol–acetone to give 4 mg of (+)-pipecolic acid, mp 269–271° dec, $[\alpha]^{22}D$ +25.8 ± 2° (*c* 0.395, water) {lit.[13] mp 268–272°, $[\alpha]^{24}D$ +27° (*c* 0.13, water)}, mmp 269–271° with reference D-(+)-pipecolic acid, mmp 252–257° with reference L-(−)-pipecolic acid.

DL-Pipecolic Acid from *meso*-1,3-Bis(2-piperidyl)-2-propanone Dihydrochloride.—*meso*-1,3-Bis(2-piperidyl)-2-propanone dihydrochloride (104 mg) was oxidized as above and the pipecolic acid isolated (6.5 mg) was recrystallized from methanol–acetone to yield 4.2 mg of DL-pipecolic acid, mp 270–272°, mmp 270–272° with reference DL-pipecolic acid.

ORD Data.—ORD data for the following compounds are listed: (+)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride (*c* 0.205, CH_3OH), $[\phi]^{29}_{400}$ +211°, $[\phi]_{300}$ +478°, $[\phi]_{250}$ +1013°, $[\phi]_{230}$ +1233°, $[\phi]_{215}$ +1630°; (+)-1,3-bis(2-piperidyl)-2-propanone, $[\phi]^{29}_{400}$ +148°, $[\phi]_{345}$ +192°, $[\phi]_{318}$ +138°, $[\phi]_{300}$ +255°, $[\phi]_{280}$ +468°, $[\phi]_{265}$ +569° (broad peak), $[\phi]_{250}$ +468°, $[\phi]_{230}$ +349°; (−)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride (*c* 0.260, CH_3OH), $[\phi]^{29}_{400}$ −196°, $[\phi]_{300}$ −363°, $[\phi]_{250}$ −841,° $[\phi]_{230}$ −1113°, $[\phi]_{215}$ −1457°; (−)-1,3-bis(2-piperidyl)-2-propanone, $[\phi]^{29}_{400}$ −138°, $[\phi]_{345}$ −198°, $[\phi]_{318}$ −129°, $[\phi]_{300}$ −231°, $[\phi]_{280}$ −396°, $[\phi]_{265}$ = −440° (broad trough), $[\phi]_{250}$ −378°, $[\phi]_{230}$ −310°; (−)-pipecolic acid from oxidation of (+)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride (*c* 0.323, H_2O), $[\phi]^{27.6}_{400}$ −40°, $[\phi]_{300}$ −62°, $[\phi]_{270}$ −76°, $[\phi]_{238}$ 0°, $[\phi]_{223}$ +136° (peak), $[\phi]_{215}$ −40°; L-(−)-pipecolic acid (standard) (*c* 0.380, H_2O), $[\phi]^{27.6}_{400}$ −37.4°, $[\phi]_{300}$ −57.7°, $[\phi]_{270}$ −64.5°, $[\phi]_{238}$ 0°, $[\phi]_{223}$ +139.5° (peak), $[\phi]_{215}$ −34°; (+)-pipecolic acid from oxidation of (−)-1,3-bis(2-piperidyl)-2-propanone dihydrochloride (*c* 0.395, H_2O), $[\phi]^{27.6}_{400}$ +32.8°, $[\phi]_{300}$ +66.5°, $[\phi]_{270}$ +75°, $[\phi]_{238}$ 0°, $[\phi]_{223}$ −147° (trough), $[\phi]_{215}$ +13°; D-(+)-pipecolic acid (standard) (*c* 0.419, H_2O), $[\phi]^{27.6}_{400}$ +35.5°, $[\phi]_{300}$ +61.5°, $[\phi]_{270}$ +77°, $[\phi]_{238}$ 0°, $[\phi]_{223}$ −144.5° (trough), $[\phi]_{215}$ +27.7°.

Registry No.—**5**, 19519-46-1; **6**, 19519-47-2; **7**, 19519-48-3; **8**, 19519-49-4; **9**, 19519-50-7; **10**, 19519-51-8; **13**, 19519-52-9; **14**, 19519-54-1; (+)-1,3-bis(2-piperidyl)-2-propanone, 19519-53-0; (−)-1,3-bis(2-piperidyl)-2-propanone, 19519-55-2; L-(−)-pipecolic acid, 3105-95-1; D-(+)-pipecolic acid, 1723-00-8.

Acknowledgment.—Sincere thanks are due Dr. G. Lyle, University of New Hampshire, for her assistance in the ORD measurements.

(12) 0.19% ninhydrin in 1-butanol–10% acetic acid (95:5).

(13) H. C. Beyerman, L. Maat, A. Van Veen, A. Zweistra and W. von Philipsborn, *Rec. Trav. Chim. Pays-Bas*, **84**, 1367 (1965).