N-Methyl-N-propyl-9-(1,4,5,6,7,7-hexachlorobicyclo[2.2.1]-5-hepten-2-yl)nonanamide (16, Table I) was prepared by reaction of N-methyl-N-propyl-10-undecenamide (I) with hexachlorocyclopentadiene (II). The former (I) was prepared by the reaction of 10-undecenoyl chloride with N-methylpropylamine in the usual manner.

I (7 g, 0.03 mol) and II (8 g, 0.03 mol) were allowed to react for 10 hr at 135°, after which the mixture was dissolved in MeOH and filtered. The MeOH and unreacted hexachlorocyclopentadiene were removed by distillation at reduced pressure. Unadducted amide was removed by the urea complex method of Swern.[7]

Hexachlorocyclopentadiene Adduct of Oleoyl Chloride (III).—Oleoyl chloride (80 g, 0.27 mol) and II (145.2 g, 0.53 mol) were allowed to react under N_2 in a flask equipped with a condenser for 28 hr at 135° as previously described for the petroselinic acid adduct.[8]

N-[8-(1,4,5,6,7,7-Hexachloro-3-octylbicyclo[2.2.1]-5-hepten-2-yl)octanoyl]-N'-methylpiperazine (7, Table I).—Compound III (25.6 g, 0.05 mol) was added to a vigorously stirred PhH solution containing 5 g (0.05 mol) of N-methylpiperazine and 5.1 g (0.05 mol) of Et_3N. Stirring was continued for an additional hour. The mixture was filtered, after which the filtrate was dried (Na_2SO_4), percolated through activated alumina, and stripped. Remaining unadducted amide was removed by the urea complex method of Swern.[7] The stripped product was dissolved in $CHCl_3$, filtered, and stripped.

N,N-Dibutyl-8-(1,4,5,6,7,7-hexachloro-3-octylbicyclo[2.2.1]-5-hepten-2-yl)octanamide (15, Table I).—Compound III (57 g, 0.1 mol) was added dropwise to a vigorously stirred PhH solution containing 14.6 g (0.11 mol) of Bu_2NH and 11.4 g (0.11 mol) of Et_3N. Stirring was continued for an additional hour. The mixture was filtered and the filtrate was washed (dilute HCl, H_2O), dried (Na_2SO_4), percolated through activated alumina, and stripped. Remaining unadducted amide was removed by the urea complex method of Swern. The stripped product was dissolved in hexane, washed (HCl, H_2O), dried (Na_2SO_4), filtered, and stripped.

The remaining amides were prepared by interaction of equimolar proportions of the respective acid chloride adduct and amine as described for the N,N-Bu_2 derivative.

Screening on agar plates by a method previously described[5] revealed that most of the compounds tabulated in Table I showed slight to moderate activity against one or more of the following organisms: *Bacillus sp., Pseudomonas sp., Aspergillus flavus, Candida albicans, Microsporum gypseum, Trichophyton rubrum,* and *T. violaceum.*

(7) D. Swern, in "Fatty Acids," K. S. Markley, Ed., Part III, Interscience Publications, Inc., New York, N. Y., 1964, p 2309.

(8) J. P. Moreau, R. L. Holmes, and G. Sumrell, *J. Amer. Oil Chemists' Soc.*, **43**, 33 (1966).

4-Desmethyltrichocereine

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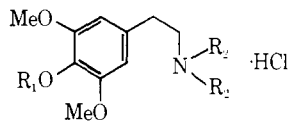
The preferential cleavage of the middle of three vicinal OMe aromatic groups[1,2] has been applied to the alkaloid trichocereine (**1**) to afford 4-desmethyltrichocereine (**2**) which was identical with the tertiary amine obtained from 4-desmethylmescaline (**3**)[1a] by conventional means.

(1) (a) A. Brossi and S. Teitel, *Org. Prep. Proc.*, **1**, 171 (1969); (b) *Helv. Chim. Acta*, **52**, 1228 (1969); (c) M. Kohn, C. Keller-Juslén, and A. von Wartburg, *ibid.*, **52**, 944 (1969); (d) T. Kametani, N. Wagatsuma, and F. Sasaki, *Yukugaku Zasshi*, **10**, 913 (1966).

(2) (a) O. Yonemitsu, H. Nakai, Y. Kanaoka, I. L. Karle, and B. Witkop, *J. Amer. Chem. Soc.*, **91**, 4591 (1969); (b) C. F. Wilcox, Jr., and M. A. Seager, *J. Org. Chem.*, **34**, 2319 (1969); (c) R. G. Wilson and D. H. Williams, *J. Chem. Soc., C*, 2475 (1968).



1, R_1, R_2 = Me
2, R_1 = H; R_2 = Me
3, R_1, R_2 = H

Experimental Section[3]

4-Desmethyltrichocereine Hydrochloride (2). A. From 1.—A solution of 3 g (11 mmol) of trichocereine·HCl (**1**), obtained by the reductive condensation of mescaline with CH_2O[4] (see procedure below), in 60 ml of 20% HCl was refluxed for 2 hr and evaporated at 50° under reduced pressure. The residue was crystallized from EtOH-Et_2O to give 2.1 g (74%) of **2**, mp 215–216°; R_f 0.52; uv max (EtOH) 230 mμ (ε 7450) (sh), 273 (1300); uv max (1 N KOH) 240 (7800) (sh), 285 (2450); nmr δ 2.78 [$N^+(CH_3)_2$], 3.77 (2 CH_3O), 6.53 (aromatics), 8.18 (OH). *Anal.* ($C_{12}H_{19}NO_3$·HCl) C, H.

B. From 3.—To a soln of 1.1 g (4.7 mmol) of 4-desmethylmescaline (**3**)[1a] in 10 ml of MeOH was added 260 mg (4.8 mmol) of NaOMe followed by 3 ml of 37% CH_2O. The mixture, after storage overnight at 25°, was hydrogenated in the presence of 500 mg of Raney Ni at 3.5 kg/cm² and 25° and filtered. The filtrate was evaporated, the residue extracted (C_6H_6), the extract was acidified with ethanolic HCl and evaporated, and the residue crystallized from EtOH-Et_2O to give 1.1 g (90%) of **2**, mp 215–216°; identical in mixture melting point, tlc, uv, and nmr with **2** obtained from **1**.

Acknowledgments.—We are grateful to Mr. J. O'Brien for technical assistance and to Professor G. Buchi, Massachusetts Institute of Technology, for fruitful discussions.

(3) Melting points (corrected) were taken in open capillary tubes with a Thomas–Hoover melting apparatus. Tlc employed silica gel G plates developed for 15 cm with EtOAc–MeOH–concentrated NH_4OH (100:10:1) and detected with Dragendorff's reagent. Uv spectra were measured with a Cary Model 14M spectrophotometer and the nmr spectra were obtained with a JEOLCO C-60H instrument using DMSO-d_6 and Me_4Si as internal standard.

(4) For alternate, multistep syntheses, see L. Reti and J. A. Castrillón, *J. Amer. Chem. Soc.*, **73**, 1767 (1951), and F. Benington, R. D. Morin, and L. C. Clark, Jr., *J. Org. Chem.*, **22**, 227 (1957).

Quaternization Products of S-(−)-Nicotine

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The following selectively quaternized S-(−)-nicotine derivatives have been synthesized for neuromuscular junction activity studies.

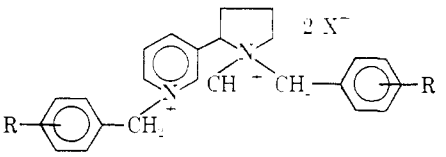
Experimental Section

Microanalyses were performed by Midwest Microlab Inc., Indianapolis, Ind. Where analyses are indicated only by elemental symbols, analytical results for those elements were within ±0.4% of theoretical values.

Bis-p-methylbenzyl-S-(−)-nicotinium Diiodide.—A mixture of 1.6 g (0.01 mol) of S-(−)-nicotine and 3.9 g of α-bromo-p-xylene was warmed to effect solution. After 24 hr an amber glass developed which showed no contamination with unreacted S-(−)-nicotine. It was dissolved in MeOH and treated with 15 ml of MeI. After 72 hr crystalline diiodide precipitated. The product was crystallized from MeOH-C_6H_6 to yield 3.0 g (48%).

Related bisbenzyl-*S*-(−)-nicotinium dihalides are listed in Table I.

TABLE I
SUBSTITUTED BISBENZYL-*S*-(−)-NICOTINIUM DIHALIDES



No.	R	Mp,[a]	Yield, %	Empirical formula
1	H	213–215	32	$C_{24}H_{28}I_2N_2$
2	*p*-Br	241–242	15	$C_{24}H_{26}Br_2I_2N_2$
3	*p*-Cl	250–251	15	$C_{24}H_{26}Cl_2I_2N_2$
4	*p*-F	255	38	$C_{24}H_{26}F_2I_2N_2$
5	*p*-NO_2	229–232	80	$C_{24}H_{26}Br_2N_4O_4$
6	*p*-CH_3	222–225	48	$C_{26}H_{32}I_2N_2$
7	*o*-CH_3	193–195	58	$C_{26}H_{32}I_2N_2$
8	*m*-CH_3	207–209	30	$C_{26}H_{32}I_2N_2$

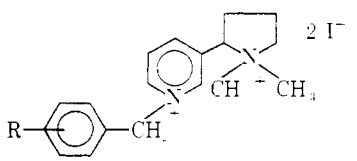
[a] Corrected melting point in °C.

Isomeric *N,N'*-methyl-substituted benzyl derivatives of *S*-(−)-nicotine were synthesized by controlled quaternizations involving reaction first on the pyridine nitrogen (N) and then on the pyrrolidine nitrogen (N'). Quaternizations on the pyridine N were effected by conducting the reactions in AcOH; the N' nitrogen was subsequently quaternized in MeOH.

***N*-*p*-Fluorobenzyl-N'-methyl-*S*-(−)-nicotinium Diiodide.**—A solution of 1.6 g (0.01 mol) of redistilled *S*-(−)-nicotine in 25 ml of glacial AcOH was mixed with 1.5 g of *p*-fluorobenzyl chloride. After 32 hr the solvent was evaporated under vacuum to yield crude and hydroscopic *N*-*p*-fluorobenzyl-*S*-(−)-nicotinium chloride which was extracted with three 25-ml fractions of Et_2O to remove unreacted materials. The crude product was dissolved in MeOH and treated with 4.3 g (0.03 mol) of MeI for 12 hr. It was chromatographed on 50 g of Woelm Activity Grade I neutral Al_2O_3 and eluted with 10–50% of MeOH–C_6H_6 to yield 2.1 g (39%) of product.

The compounds in Table II were prepared similarly.

TABLE II
SUBSTITUTED
N-BENZYL-*N'*-METHYL-*S*-(−)-NICOTINIUM DIIODIDES



No.	R	Mp,[a]	Yield, %	Empirical formula
9	H	210–212	73	$C_{18}H_{24}I_2N_2$
10	*p*-Br	247–248	41	$C_{18}H_{23}BrI_2N_2$
11	*p*-Cl	235–237	40	$C_{18}H_{23}ClI_2N_2$
12	*p*-F	221–223	39	$C_{18}H_{23}FI_2N_2$
13	*p*-NO_2	225–227	23	$C_{18}H_{23}I_2N_3O_2$
14	*p*-CH_3	225–227	16	$C_{19}H_{26}I_2N_2$
15	*o*-CH_3	205–208	76	$C_{19}H_{26}I_2N_2$
16	*m*-CH_3	170–172	72	$C_{19}H_{26}I_2N_2$

[a] Corrected melting point in °C.

The substituted *N*-methyl-*N'*-benzyl-*S*-(−)-nicotine dihalides (Table III) were prepared in an analogous fashion by conducting the first quaternization with MeI and further treating the product with the appropriate benzyl halide. In those instances where diiodides were obtained the products resulted from halogen exchange.

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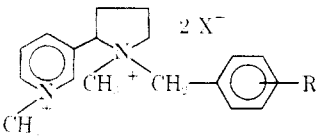
TABLE III
SUBSTITUTED
N-METHYL-*N'*-BENZYL-*S*-(−)-NICOTINIUM DIHALIDES



No.	R	Mp,[a]	Yield, %	Empirical formula
17	H	190–193	41	$C_{18}H_{24}BrIN_2 \cdot 0.5H_2O$
18	*p*-Br	175–178	61	$C_{18}H_{23}Br_2IN_2$
19	*p*-Cl	217–219	30	$C_{18}H_{23}ClIN_2$
20	*p*-F	226–229	24	$C_{18}H_{23}FIN_2$
21	*p*-NO_2	209–211	93	$C_{18}H_{23}BrIN_3O_2 \cdot H_2O$
22	*p*-CH_3	156–161	57	$C_{19}H_{26}BrIN_2 \cdot 2H_2O$
23	*o*-CH_3	188–190	28	$C_{19}H_{26}IN_2$
24	*m*-CH_3	219–223	68	$C_{19}H_{26}IN_2$

[a] Corrected melting point in °C.

1-Arylsulfonylhydrazides. III. 4-Phenyl-1-arylsulfonylthiosemicarbazides and 2-Arylsulfonylhydrazone-3-phenyl-4-thiazolines[1]

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As a continuation of our investigation of derivates of the 1-arylsulfonylhydrazides, we now wish to report the preparation of two new series, the 4-phenyl-1-arylsulfonylthiosemicarbazides (Ia–c) and the 2-arylsulfonylhydrazone-3-phenyl-4-thiazolines (IIa–f).

The 1-arylsulfonylthiosemicarbazides have been evaluated as fungicides[2,3] and as bacteriostatic agents.[3,4] Compounds containing the thiazoline ring have been

TABLE I
$ArSO_2NHNHCSNHC_6H_5$

Compd	Ar	Mp, °C[a] dec	Yield, %[b]	Formula
Ia	*p*-$CH_3OC_6H_4$	170–171	88	$C_{14}H_{15}N_3O_3S_2$
Ib	*p*-$C_2H_5OC_6H_4$	177–178	86	$C_{15}H_{17}N_3O_3S_2$
Ic	*p*-*n*-$C_3H_7OC_6H_4$	162–163	80	$C_{16}H_{19}N_3O_3S_2$

[a] The melting points were determined in open capillary tubes and are uncorrected. [b] The yields are based on the product after the first recrystallization. [c] All analytical results were within ±0.3% of the theoretical values. All compounds were analyzed for C, H, N, S.

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