General Procedures.—The products were prepared by condensing equimolar amounts of the appropriate 2-aminobenzamide or 2-aminobenzohydroxamic acid and of the aldehyde or ketone in absolute EtOH at room (**43**, **65**, **68**) or at boiling (**63**, **64**) temperature, in boiling aqueous EtOH in the presence of NaOH (**1**, **6**, **11**, **16**, **21**, **32**, **43**, **45**, **50**, **55**, **60**, **71**), or in boiling absolute EtOH in the presence of piperidine (**74**), dry HCl (**78**), or NaOEt (remaining products). Work-up followed as usual.

3-*N*,*N*-Disubstituted Aminoethoxy-2,3-dihydro-4(1H)-quinazolinones. General Procedure.—To 1 mol of the K salt of the 3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in *i*-PrOH, 1 mol of 2-dialkylaminoethyl chloride was added. The mixture was refluxed for 3–4 hr and filtered from KCl. The products either crystallized directly or were obtained by concentration. Recrystallization from an appropriate solvent gave pure bases except **72** and **76**, for which only the hydrochloride salts fulfilled the analytical requirements.

3-Carbalkoxymethoxy-2,3-dihydro-4(1H)-quinazolinones. General Procedure.—To a solution of 3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in 1 equiv of alcoholic KOH 1 equiv of alkyl bromoacetate was added and the mixture was allowed to stand till the product separated; **77** was obtained on dilution with H_2O.

2-Phenyl-3-carboxymethoxy-2,3-dihydro-4(1H)-quinazolinone (**42**) was obtained by hydrolysis at room temperature of the ester **41** with 1 equiv of methanolic KOH, work-up as usual.

2-Phenyl-3-benzoyloxy-2,3-dihydro-4(1H)-quinazolinone (**39**) was obtained by Schotten-Baumann acylation of 2-phenyl-3-hydroxy-2,3-dihydro-4(1H)-quinazolinone.

2-Phenyl-3-benzyloxy-2,3-dihydro-4(1H)-quinazolinone (**36**).—To a solution of 2.4 g (0.01 mol) of 2-phenyl-3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in 10 ml of methanolic 1 *N* KOH 1.3 g (0.01 mol) of $PhCH_2Cl$ was added. The mixture was refluxed for 1 hr and the product separated on cooling. In a similar way **2,2-dimethyl-3-benzyloxy-2,3-dihydro-4(1H)-quinazolinone** (**81**) was obtained after dilution with H_2O of the reaction mixture.

2-Phenyl-3-allyloxy-2,3-dihydro-4(1H)-quinazolinone (**37**).—To a solution of 2.8 g (0.01 mol) of the potassium salt of 2-phenyl-3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in 10 ml of DMF 0.8 g (0.01 mol) of allyl bromide was added. The reaction mixture was set for 4 hr at room temperature and then poured into H_2O. The separated oil was extracted in $CHCl_3$, and the extract was washed (H_2O), dried, and evaporated to give crude **37**. Similarly, **2-phenyl-3-propargyloxy-2,3-dihydro-4(1H)-quinazolinone** (**38**) was prepared.

Hexachlorocyclopentadiene Adducts of Unsaturated Amides

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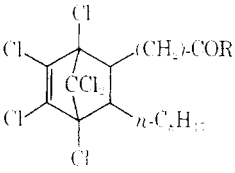
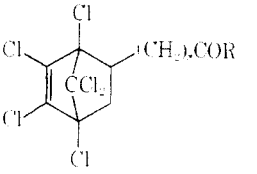
It was previously shown that monoolefinic compounds react with hexachlorocyclopentadiene to give Diels–Alder adducts, some of which have exceptional insecticidal activity.[2] Previous publications[3–5] from this laboratory have shown that many long chain amides possess antimycotic activity. In continuing these investigations a number of hexachlorocyclopentadiene adducts of unsaturated amides have been prepared and are presented in Table I.

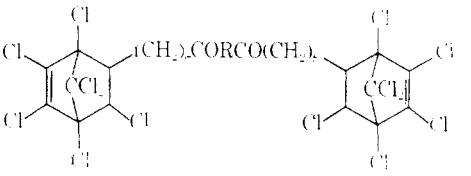
TABLE I



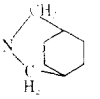
1–15



16, and **17**



18

No.	R	n^{30}D	Density at 30°	Formula[a]
1	$N(CH_3)_2$		1.4534	$C_{21}H_{24}Cl_6NO$
2		1.5134	1.4593	$C_{25}H_{28}Cl_6NO$
3	$N(C_2H_5OCH_3)_2$	1.4943	1.4266	$C_{25}H_{32}Cl_6NO_3$
4		1.5166	1.4132	$C_{25}H_{28}Cl_6NO_2$
5		1.5118	1.4521	$C_{23}H_{24}Cl_6NO$
6		1.5213	1.4675	$C_{24}H_{27}Cl_6NO$
7		1.5157	1.4698	$C_{23}H_{24}Cl_6N_2O$
8	$N(C_2H_5)_2$	1.5031	1.4385	$C_{21}H_{24}Cl_6NO$
9	$N(C_2H_5)(CH_2)_3OC_2H_5$	1.4997	1.4337	$C_{24}H_{30}Cl_6NO_2$
10	$N(CH_3)$-*n*-C_4H_9	1.5043	1.4407	$C_{23}H_{26}Cl_6NO$
11	$N(CH_3)CH_2CH{=}CH_2$	1.5106	1.4618	$C_{23}H_{24}Cl_6NO$
12	$NHCH_2CH{=}CH_2$	1.5156	1.4922	$C_{22}H_{22}Cl_6NO$
13	$NHCH_2C_6H_5$	1.5346	1.2202	$C_{26}H_{24}Cl_6NO$
14		1.5212	1.2213	$C_{27}H_{24}Cl_6NO$
15	N(*n*-C_4H_9)$_2$	1.5048	1.1441	$C_{25}H_{34}Cl_6NO$
16	$N(CH_2CH_2CH_2CH_3)_2$	1.5141	1.2455	$C_{25}H_{32}Cl_6NO$
17		1.5322	1.3088	$C_{27}H_{28}Cl_6NO$
18		1.5409	1.3115	$C_{30}H_{36}Cl_{12}N_2O_2$

[a] All compounds were analyzed for N, and the analytical values were within ±0.4% of the calculated values.

Experimental Section[6]

The densities were determined by pycnometer in a thermostated bath controlled to within 0.1°. Refractive indices were measured at 30.0 ± 0.1° with a precision Bausch and Lomb refractometer using the D Na line.

(1) A laboratory of the Southern Utilization Research and Development Division, ARS, USDA. Naming a company or product does not imply approval or recommendation by the Department over others which may also be suitable.

(2) E. K. Fields, *J. Amer. Chem. Soc.*, **76**, 2709 (1954).

(3) A. F. Novak, G. C. Clark and H. P. Dupuy, *J. Amer. Oil Chemists' Soc.*, **38**, 321 (1961).

(4) A. F. Novak, M. J. Fisher, S. P. Fore, and H. P. Dupuy, *ibid.*, **41**, 503 (1964).

(5) A. F. Novak, J. M. Sidar, R. R. Mod, F. C. Magne, and E. L. Skau, *ibid.*, **46**, 249 (1969).

(6) Micro analyses are by Galbraith Laboratories, Knoxville, Tenn.

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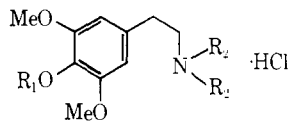
The preferential cleavage of the middle of three vicinal OMe aromatic groups[1,2] has been applied to the alkaloid trichocereine (**1**) to afford 4-desmethyltrichocereine (**2**) which was identical with the tertiary amine obtained from 4-desmethylmescaline (**3**)[1a] by conventional means.

(1) (a) A. Brossi and S. Teitel, *Org. Prep. Proc.*, **1**, 171 (1969); (b) *Helv. Chim. Acta*, **52**, 1228 (1969); (c) M. Kuhn, C. Keller-Juslén, and A. von Wartburg, *ibid.*, **52**, 944 (1969); (d) T. Kametani, N. Wagatsuma, and F. Sasaki, *Yakugaku 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.* ($C_{12}H_{19}NO_3 \cdot HCl$) 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%).