2-(3,3-Diphenylallyl)-1,2,3,4-tetrahydroisoquinoline (46) was prepared from the corresponding tertiary alcohol, as described above. The **base** was crystallized from isopropyl alcohol, m.p. 83–84°.

Anal. Calcd. for $C_{24}H_{23}N$: C, 88.6; H, 7.12; equiv. wt., 325. Found: C, 87.6; H, 7.14; equiv. wt., 323.

The **maleate** crystallized from ethanol; m.p. 174–175°.

Anal. Calcd. for $C_{24}H_{23}N \cdot C_4H_4O_4$: C, 76.2; H, 6.16; equiv. wt., 441.5. Found: C, 76.1; H, 6.12; equiv. wt., 441.

1-(4-Fluorophenyl)-1-phenyl-4-(N-phenethyl-N-methylamino)-1-butene (47).—The base was obtained as a viscous oil by dehydrating the corresponding tertiary alcohol with 85% H_2SO_4. The **maleate** crystallized from isopropyl alcohol–petroleum ether (b.p. 60–80°), m.p. 125–127°.

Anal. Calcd. for $C_{25}H_{26}FN \cdot C_4H_4O_4$: C, 73.4; H, 6.2; N, 2.95. Found: C, 73.5; H, 6.4; N, 3.2.

1-Benzoyloxy-1,1-diphenyl-2-methyl-3-pyrrolidylpropane (48).—To a solution of 1,1-diphenyl-2-methyl-3-pyrrolidyl-propan-1-ol (29.6 g., 0.1 mole) in a mixture of dry benzene (150 ml.) and dry ether (100 ml.) was added with cooling (0–5°) benozyl chloride (7 g., 0.05 mole). The mixture was allowed to stand at room temperature for 72 hr. The hydrochloride of the starting material was filtered, final traces being removed by washing with water. After drying, the solvents were distilled to leave a colorless viscous oil, which was converted to the **oxalate** salt. This was purified by crystallization from isopropyl alcohol, m.p. 170–172°, yield 7.1 g. (28%).

Anal. Calcd. for $C_{27}H_{29}NO_2 \cdot C_2H_2O_4$: C, 71.1; H, 6.38; N, 2.8. Found: C, 71.2; H, 6.50; N, 2.7.

1-Benzoyloxy-1,1-diphenyl-2-methyl-3-piperidylpropane (49) was prepared by treating the corresponding tertiary alcohol with benzoyl chloride; it crystallized from isopropyl alcohol as colorless prisms, m.p. 165–167°.

Anal. Calcd. for $C_{28}H_{31}NO_2$: C, 81.3; H, 7.56; N, 3.4. Found: C, 81.5; H, 7.68; N, 3.5.

1,1-Diphenyl-2-methyl-3-pyrrolidyl-1-propionyloxypropane (50).—A mixture of 1,1-diphenyl-2-methyl-3-pyrrolidylpropan-1-ol (3.0 g., 0.01 mole), pyrridine (4.0 ml.), and propionic anhydride (4.0 ml. 0.03 mole) was heated on a steam bath for 3 hr. The solvent was distilled *in vacuo* and the residual oil converted into its **oxalate**. Crystallization from ethyl alcohol–water gave the pure ester, m.p. 170–173°.

Anal. Calcd. for $C_{23}H_{29}NO_2 \cdot C_2H_2O_4$: C, 68.0; H, 7.08; equiv. wt., 220.8. Found: C, 67.7; H, 7.19; equiv. wt., 214.

3-Dimethylamino-1,1-diphenyl-2-methyl-1-propionoxypropane (51) was prepared from the corresponding tertiary alcohol (**1**) and propionic anhydride.[19] The oxalate crystallized from ethyl alcohol–water as colorless prisms, m.p. 152–153°.

Anal. Calcd. for $C_{21}H_{27}NO_2 \cdot C_2H_2O_4 \cdot 0.5H_2O$: C, 65.0; H, 7.12; N, 3.3. Found: C, 65.5; H, 7.38; N, 3.4.

The hydrochloride was characterized by Perrine.[19]

1-Benzoyloxy-3-dimethylamino-1,1-diphenyl-2-methylpropane (52) was prepared from the corresponding tertiary alcohol (**1**) and benzoyl chloride. The **base** crystallized from isopropyl alcohol as colorless prisms, m.p. 115–116°.

Anal. Calcd. for $C_{25}H_{27}NO_2$: C, 80.4; H, 7.29; N, 3.75. Found: C, 80.7; H, 7.51; N, 3.80.

(19) T. D. Perrine, *J. Org. Chem.*, **18**, 898 (1953).

Synthesis and Cholinergic Effects of Certain N-Methoxylated Quaternary Compounds[1a]

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Analogs of acetylcholine, methacholine, carbachol, and bethanechol have been prepared, in which one of the N-methyl groups has been replaced by methoxy. Biological data are presented on these compounds.

The biological actions of the quaternary alkoxyamine moiety have not been studied thoroughly or systematically; the literature contains relatively few reports of testing of alkoxy analogs of quaternary ammonium drugs for their systemic effects. The chemical similarity between the alkylamino and the alkoxyamino groups suggests that organic molecules containing these moieties may be adsorbed at many of the same receptor sites in the body; differences in bulk and in electronic distribution may in some instances result in differences in the responses of the body to the two classes of compounds. Thus, it is possible that certain alkoxyamine derivatives may possess therapeutic advantages over their amine analogs.

Major and Hess[2] found that a quaternary N-methoxy congener of methantheline had atropine-like activity similar to methantheline itself. Rogers, *et al.*,[3] found that methoxy-, ethoxy-, or *n*-propyloxytrimethylammonium cations closely resemble their alkyltrimethylammonium counterparts in muscarinic properties. Palazzo and co-workers[4] reported that 1,10-bis(dimethylaminooxy)decane dimethiodide possessed anticholinesterase activity. Bruno, *et al.*,[5] found that 2-dimethylaminooxyethyl acetate methiodide (V) had similar biological activity to acetylcholine, and Schiatti and Maffii[6] reported that this compound was equal to 3-dimethylaminopropyl acetate methiodide as a substrate for acetylcholinesterase; although both were poorer substrates than acetylcholine, they were of the same order.

In the present work, certain significant structural variations in the acetylcholine molecule have been applied to the N-methoxy congeners. Thus, the N-methoxy analogs of acetylcholine (Ia), methacholine (IIa), carbachol (IIIa), and bethanechol (IVa) have

(1) (a) This investigation was supported in part by Grant GM-10753, National Institute of General Medical Sciences, and in part by Grant B-1396, United States Public Health Service. (b) To whom all correspondence should be addressed.

(2) R. T. Major and H. J. Hess, *J. Med. Pharm. Chem.*, **2**, 461 (1960).

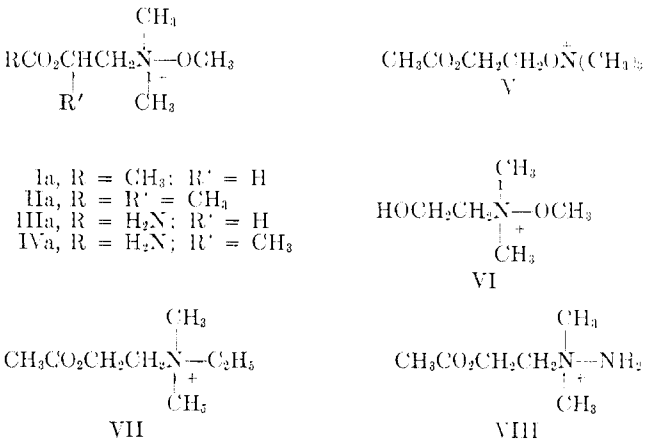
(3) E. F. Rogers, D. Bovet, V. G. Longo, and G. B. Marini-Bettolo, *Experientia*, **9**, 260 (1953).

(4) G. Palazzo, E. F. Rogers, and G. B. Marini-Bettolo, *Gazz. chim. ital.*, **84**, 915 (1954).

(5) I. Bruno, B. J. R. Nicolaus, G. Pagani, and E. Testa, *Helv. Chim. Acta*, **45**, 358 (1962).

(6) P. Schiatti and G. Maffii, *Boll. Soc. Ital. Biol. Sper.*, **38**, 1823 (1962).

been prepared. (The designations I, II, III, and IV will be employed hereafter to designate the parent trimethylammonium structures.) Jones and Major[7] prepared 2-hydroxyethyldimethylmethoxyammonium iodide (VI) and mentioned the possible biological significance of it and of its acetate ester (Ia), as analogs of choline and acetylcholine. A search of the literature has not revealed that the acetate ester (Ia) of VI has been prepared, or that VI has been subjected to biological testing. Inspection of Catalin models indicates that the cationic heads of Ia and of N-methyl-N-ethyl-2-aminoethyl acetate methiodide (VII) are almost identical in bulk. It has been concluded[8] that the nitrogen atom does not expand its valence shell to accommodate more than eight electrons; therefore, the trialkylalkoxyammonium cation must resemble a tetraalkylammonium cation in localization of the positive charge. It would be expected that Ia and VII would demonstrate qualitatively and quantitatively similar biological properties. Holton and Ing[9] found that VII had from one-half to one-fifth the muscarinic activity of acetylcholine. The hydrazinium analog (VIII) of acetylcholine was reported[10] to be much less potent than acetylcholine.



Materials and Methods

Pharmacology. Muscarinic Potency Ratios.—Mongrel dogs of either sex, weighing 7–20 kg., were anesthetized with 15 mg./kg. of thiopental sodium and 250 mg./kg. of barbital sodium, administered intravenously. Artificial ventilation was provided by tracheal cannulation, and carotid artery blood pressure was measured by a Statham pressure transducer and recorded with an Offner Type RS dynograph. Drugs were injected in volumes of 0.05–0.5 ml. into the femoral vein. In preliminary experiments in three other dogs, a log interval of 0.6 between high and low doses was found to be satisfactory and on a linear portion of the dose–response curve; also, approximate relative doses of the four parent drugs and their N-methoxy derivatives were determined. The relative potencies were then obtained using a 2 × 2 parallel line assay,[11] employing 17 dogs. Doses of the compounds in all experiments were based on weight of the cation employed, and the sequences of all administrations were derived from a table of random numbers.[12] Absolute depressor responses obtained with fresh aqueous solutions of the compounds were tabulated and potency ratios determined. The arterial pressure was allowed to return to preinjection levels in each case following drug administration before the next compound was injected. Potencies are compared with the standard, acetylcholine.

Guinea pigs were sacrificed by cervical dislocation and 4–6 cm. sections of ileum were placed in a Lucite chamber and superfused with Krebs' bicarbonate buffer solution, aerated with O_2–CO_2 (95:5). Measurements of isometric tension were obtained by a Statham force transducer and recorded by a Gilson Medical Electronics polygraph. Preliminary experiments revealed approximately equal doses of drugs and linearity of the dose–response curve; a log dose interval of 1.0 was employed. The bioassay (2 × 2) was then performed, using ileum sections from 23 animals, doses of acetylcholine were applied from a microsyringe until uniform contractions developed, then the drugs were applied in the same manner in random order.

Neostigmine Potentiation.—Six dogs were prepared as described above, except that blood pressure was recorded from a femoral artery. Neostigmine sulfate, 50 γ/kg., was administered slowly intravenously following control doses of the following cholinergic agents: acetylcholine (I), its methoxy analog (Ia), bethanechol (IV), its methoxy analog (IVa), methoxycarbachol (IIIa), and methoxymethacholine (IIa). When blood pressure had returned to preneostigmine levels, the same doses of the drugs were injected as before. Responses were recorded as absolute falls in femoral artery blood pressure. Data from this experiment were analyzed by the Student's t test, paired comparison.[12]

Nicotinic Studies.—Six dogs were prepared as above; blood pressure was recorded from the carotid artery. Atropine sulfate, 1.5 mg./kg. i.v., was administered to each animal and blood pressure was monitored. When the blood pressure was established at preinjection levels, doses of all drugs were given intravenously as 0.3 mg./kg. of the cations, and the maximal pressor response was recorded. Eight Dutch rabbits of either sex, weighing 1–2 kg., were anesthetized with 200 mg./kg. of phenobarbital sodium administered intravenously in the marginal ear vein. Tracheal and carotid artery cannulations were performed and blood pressure was recorded as previously. Atropine sulfate, 5.0 mg./kg., administered intramuscularly and intravenously as divided doses, was injected following completion of surgical procedures. When the blood pressure was stabilized at preinjection levels, 1.0 mg./kg. of cation of each compound was administered in random order by jugular cannula. Data from these experiments were analyzed by the Wilcoxan matched-pairs signed ranks test.[12] Nicotinic effects were recorded as absolute pressor responses.

Results

Pharmacology. Muscarinic Potency Ratios. The potency ratios as determined from dog blood pressure and the isolated guinea pig ileum, with their 95% fiducial limits, are presented in Table I, and are illustrated in Figure 1. As determined on dog blood pressure, the potency of each methoxy derivative is less than that of the parent compound, with the exception

TABLE I

POTENCY RATIOS WITH 95% FIDUCIAL LIMITS AS DETERMINED FROM 2 × 2 PARALLEL LINE BIOASSAY

Compd.	Dog blood pressure N^a = 17	Guinea pig ileum N^a = 23
Acetylcholine (I)	1.00	1.00
Methoxy analog (Ia)	0.55 (0.53–0.58)	0.51 (0.50–0.52)
Methacholine (II)	17.33 (17.00–17.66)	1.13 (1.12–1.14)
Methoxy analog (IIa)	0.14 (0.13–0.14)	0.10 (0.06–0.13)
Carbachol (III)	9.41 (8.87–9.94)	1.60 (1.59–1.61)
Methoxy analog (IIIa)	3.54 (3.47–3.61)	2.44 (2.44–2.45)
Bethanechol	0.36 (0.29–0.43)	0.09 (0.08–0.09)
Methoxy analog (IIIa)	8.04 (7.98–8.10)	1.55 (1.54–1.56)

^{a} N = the number of animals used in the assay.

(7) L. W. Jones and R. T. Major, *J. Am. Chem. Soc.*, **49**, 1527 (1927).

(8) G. W. Wheland, "Advanced Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1946, p. 423.

(9) P. Holton and H. R. Ing, *Brit. J. Pharmacol.*, **4**, 190 (1949).

(10) F. W. Schueler and C. Hanna, *Arch. intern. pharmacodyn.*, **88**, 351 (1951).

(11) D. J. Finney, "Experimental Design and its Statistical Basis," University of Chicago Press, Chicago, Ill., 1955.

(12) A. Goldstein, "Biostatistics—An Introductory Text," The Macmillan Company, New York, N. Y., 1964.

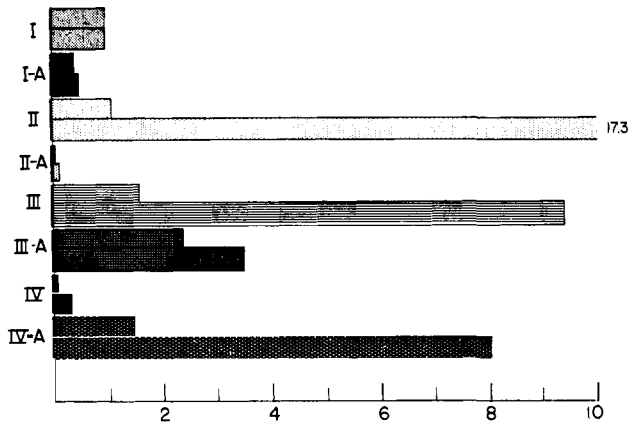


Figure 1.—Potency ratios of cholinergic agents as determined by 2 × 2 parallel line bioassay on dog blood pressure and the isolated guinea pig ileum. All compounds are compared to the standard, acetylcholine (I). Potencies greater than 1.0 indicate that the compound is more potent than I. Opposite each Roman numeral designation, the upper bar represents the potency ratio as determined on the guinea pig ileum, the lower bar as determined on dog blood pressure.

of IVa, which is 22 times more potent than the parent compound. On the superfused guinea pig ileum, Ia and IIa were less potent than the parent drugs, IIIa was slightly more potent than its parent compound, and IVa was some 17 times more potent than bethanechol. A typical table for the analysis of variance is presented in Table II, and illustrates the lack of deviation from

Table II

Analysis of Variance, 2 × 2 Parallel Line Bioassay. Acetylcholine (I) *vs.* IVa on Dog Blood Pressure Reduction, Randomized Complete Block Design[a]

	Source of variance				
	df	*SS*	*MS*	*F*	*P*
Preparations	1	390.72	390.72	3.80	N.S.
Regression	1	7,309.19	7,309.19	71.15	>0.01
Parallelism	1	2.48	2.48	>1	N.S.
Doses	3	7,702	2,567.33	24.99	>0.01
Animals (blocks)	16	7,855	490.94	4.78	>0.01
Error	48	4,931	102.73		
Total	67	20,488			

[a] N (number of animals used) = 17.

parallelism, the significant regression, and the matching of responses obtained. The dose–response curves, as obtained from the 2 × 2 parallel line bioassay, are presented in Figure 2.

Neostigmine Potentiation.—Only acetylcholine and its methoxy derivative were significantly potentiated (P = 0.05) by 50 γ/kg. of neostigmine sulfate. An illustration of this potentiation is provided in Figure 3.

Nicotinic Potency Studies.—The mean blood pressure responses obtained from the cholinergic agents employed following administration of atropine sulfate in dogs is shown in Table III. The blood pressure in

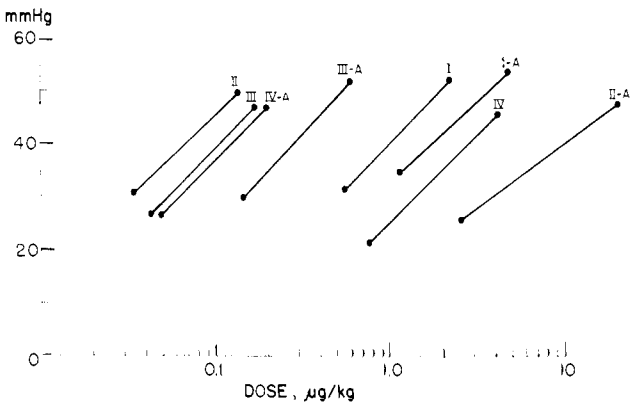


Figure 2.—Dose–response curves for cholinergic agents as obtained from 2 × 2 parallel line bioassays (N = 17).

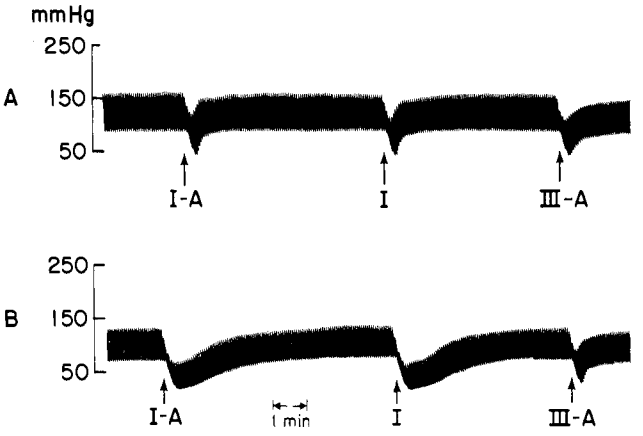


Figure 3.—Example of potentiation of dog blood pressure responses to acetylcholine (I) and N-methoxyacetylcholine (Ia) by neostigmine sulfate: A, before neostigmine; B, the same doses after neostigmine. Methoxycarbachol (IIIa) was not potentiated.

these animals was not elevated by methacholine or by its methoxy derivative. The nicotinic responses produced by the methoxy derivatives of acetylcholine and carbachol were significantly reduced from those of their parent compounds. Bethanechol had no nicotinic activity here, but methoxy substitution on the cationic head of this molecule introduced powerful nicotinic activity, as can be seen from the illustrative record shown in Figure 4. Similar results were obtained in rabbits (Table IV), except that no significant difference between acetylcholine and Ia could be demonstrated. Also, fasciculation of skeletal muscle was noted in several rabbits following the injection of carbachol and IIIa. The pressor responses observed from these agents were abolished in the dog by prior administration of 20 mg./kg. of hexamethonium chloride.

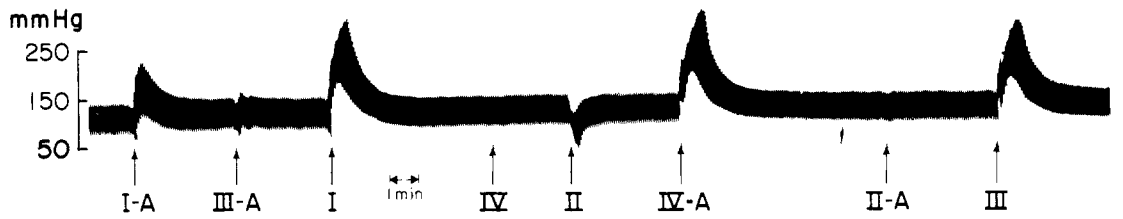


Figure 4.—Carotid blood pressure responses to equal doses of cholinergic agents in dog following administration of atropine sulfate. Note difference in responses to IV and IVa.

TABLE III

BLOOD PRESSURE ELEVATION BY CHOLINERGIC AGENTS IN DOGS FOLLOWING ADMINISTRATION OF ATROPINE SULFATE

	Dog						
Compd.	1	2	3	4	5	6	Mean
I	27	160	40	58	30	120	72.5
Ia	17	110	5	50	35	85	49.5
II	0	0	0	0	0	0	0
IIa	0	0	0	0	0	0	0
III	47	142	130	72	53	130	95.6
IIIa	5	7	0	0	0	20	5.3
IV	0	0	0	0	0	0	0
IVa	55	167	120	60	50	130	97.0

TABLE IV

RELATIVE NICOTINIC PRESSOR RESPONSES PRODUCED BY N-METHOXY DERIVATIVES AND THEIR PARENT COMPOUNDS. ANALYSIS OF DATA BY WILCOXAN MATCHED-PAIRS SIGNED RANKS TEST

Dogs, $N^a = 6$	Rabbits, $N^a = 8$
I > Ia	I = Ia
II = IIa	II = IIa
III > IIIa	III > IIIa
IV-A > IV	IVa > IV
IV-A = III > I	IVa = III > I

[a] N = number of animals used in each assay.

Experimental Section[13]

N-Methoxy-N-methyl-2-aminoethyl Acetate (IX).—Acetyl chloride (9.7 g., 0.124 mole) in 40 ml. of dry benzene was added dropwise with stirring to 18.2 g. (0.173 mole) of N-methoxy-N-methyl-2-aminoethanol[14] in 30 ml. of dry benzene. The reaction mixture was refluxed 2 hr., during which time a dark yellow oil separated. The benzene was removed under reduced pressure, and the residue (which crystallized on standing overnight) was dissolved in 50 ml. of 10% $NaHCO_3$ solution. The resulting dark red solution was extracted repeatedly with ether. The combined ether extracts were dried ($MgSO_4$) and filtered, and the ether was removed under reduced pressure. The yellow oily residue was distilled at 71–73° (16 mm.) to yield 12.5 g. (52%) of product, $n^{25}D$ 1.4100. The infrared spectrum ($CHCl_3$) showed peaks at 5.73 (C=O) and 8.2 μ (acetate C–O).

Anal. Calcd. for $C_6H_{13}NO_3$: C, 48.99; H, 8.90; N, 9.53. Found: C, 48.92; H, 8.83; N, 9.09.

N-Methoxy-N-methyl-2-aminoethyl acetate hydrochloride was recrystallized from 2-propanol–ether to yield an extremely hygroscopic white solid, m.p. 74–75°.

Anal. Calcd. for $C_6H_{14}ClNO_3$: C, 39.24; H, 7.68; Cl, 19.37; N, 7.62. Found: C, 39.13; H, 7.81; Cl, 19.20; N, 7.86.

N-Methoxy-N-methyl-1-amino-2-propanol (X).—Propylene oxide (77.0 g., 1.33 moles) in 150 ml. of methanol was added slowly with stirring to 56.2 g. (0.92 mole) of N,O-dimethylhydroxylamine (Aldrich Chemical Co.) in 50 ml. of methanol. The mixture was refluxed 16 hr., the solvent was removed under reduced pressure, and the residue was distilled at 52–55° (16 mm.), to yield 89.6 g. (82%) of a colorless liquid, $n^{25}D$ 1.4108. An infrared spectrum (film) showed a peak at 2.9 μ (OH).

Anal. Calcd. for $C_5H_{13}NO_2$: C, 50.36; H, 10.98; N, 11.17. Found: C, 50.33; H, 11.23; N, 11.58.

N-Methoxy-N-methyl-1-amino-2-propyl acetate (XI) was prepared in 59% yield by the method employed for IX; b.p. 158–160° (742 mm.), $n^{25}D$ 1.4088. An infrared spectrum (film) showed peaks at 5.73 (C=O) and at 8.05 μ (acetate C–O).

Anal. Calcd. for $C_7H_{15}NO_3$: C, 52.20; H, 9.42; N, 8.70. Found: C, 52.52; H, 9.48; N, 8.90.

N-Methoxy-N-methyl-1-amino-2-propyl acetate hydrochloride was recrystallized from 2-propanol–ether to yield an extremely hygroscopic white solid, m.p. 130–131°.

Anal. Calcd. for $C_7H_{16}ClNO_3$: C, 42.52; H, 8.15; N, 7.09. Found: C, 42.64; H, 8.68; N, 8.16.

N-Methoxy-N-methyl-2-aminoethyl Carbamate (XII).—N-Methoxy-N-methyl-2-aminoethanol (21 g., 0.2 mole) in 100 ml. of anhydrous ether was added slowly with stirring to 12.0 g. (0.15 mole) of carbamoyl chloride[15] in 25 ml. of anhydrous ether. A white solid separated, which was collected on a filter, and was added to 50 ml. of 50% KOH solution. The resulting mixture was extracted repeatedly with ether, the combined extracts were dried ($MgSO_4$) and filtered, and the ether was removed on a steam bath. The residue was distilled at 145–146° (23 mm.); the distillate solidified almost immediately; m.p. 72.5–73°, yield 7.4 g. (33%). An infrared spectrum ($CHCl_3$) showed peaks at 2.82 and 2.92 (NH), at 5.82 (C=O), and at 6.3 μ (primary amide).

Anal. Calcd. for $C_5H_{12}N_2O_3$: C, 40.60; H, 8.12; N, 18.90. Found: C, 41.11; H, 8.35; N, 18.43.

N-Methoxy-N-methyl-1-amino-2-propyl carbamate (XIII) was prepared in 29% yield by the method employed for XII; b.p. 148–154° (30 mm.), $n^{25}D$ 1.4434. The infrared spectrum (film) showed peaks at 2.88 and 2.98 (NH), at 5.82 (C=O), and at 6.25 μ (primary amide).

Anal. Calcd. for $C_6H_{14}N_2O_3$: C, 44.42; H, 8.64; N, 17.28. Found: C, 43.61; H, 8.72; N, 17.68.

TABLE V

N-METHOXYLATED QUATERNARY COMPOUNDS

$$RCO_2CHCH_2\overset{CH_3}{\underset{R'}{\overset{|}{\underset{|}{N}}}}\overset{+}{\underset{CH_3}{\overset{|}{\underset{|}{O}}}}CH_3 \cdot X^-$$

						Yield,		Calcd., %				Found, %			
No.	R	R'	X	Method	M.p., °C.	%	Formula	C	H	N	X	C	H	N	X
Ia	CH_3	H	I	A	164–165[a]	21	$C_7H_{16}INO_3$	29.05	5.58	4.85	43.89	29.07	5.84	5.33	43.87
IIa	CH_3	CH_3	Br	B	124–125[b]	31	$C_8H_{18}BrNO_3$	37.52	7.08	5.48	31.18	37.52	6.98	6.08	31.88
IIIa	H_2N	H	I	A	101–102[a]	30	$C_6H_{15}IN_2O_3$	24.85	5.23	9.66	43.71	25.24	5.33	9.57	43.59
IVa	H_2N	CH_3	I	A	195–196[b]	51	$C_7H_{17}IN_2O_3$	27.62	5.64	9.22	41.73	27.40	5.92	8.74	42.01

[a] From 2-propanol–ether. [b] From 2-propanol.

Quaternary Salts of N-Methoxyamino Esters. Method A.—The N-methoxy-N-methylaminoalkyl ester (0.03 mole) and 5 ml. of methyl iodide in 30 ml. of 2-propanol were heated in a sealed tube at 60° for 30 hr. The dark reaction mixture was kept in a refrigerator 24 hr., and the yellow crystals which separated were recrystallized repeatedly from 2-propanol–ether (see Table V).

Method B.—The N-methoxy-N-methylaminoalkyl ester (0.03 mole) was heated with 12 g. of methyl bromide in 30 ml. of acetone for 14 hr., using a Dry Ice–acetone cold finger condenser. The reaction mixture was taken to dryness under reduced pressure, and the residue was recrystallized several times from 2-propanol–ether (see Table V).

(13) All melting points are corrected and boiling points are uncorrected. Analyses are by Schwartzkopf Microanalytical Laboratories, Woodside, N. Y., and Huffman Laboratories, Wheatridge, Colo. Infrared spectra were recorded on a Beckman IR-5A spectrophotometer.

(14) R. T. Major and L. H. Peterson, *J. Org. Chem.*, **22**, 580 (1957).

(15) L. Gatterman, *Ber.*, **23**, 1190 (1890).