ferred to a Claisen flask it was subjected to a pyrolytic distillation under 20 mm. pressure. The oily product was dissolved in ether and washed with dilute hydrochloric acid. The ether solution was dried and concentrated and the residue distilled 50–55° at 3 mm. pressure. Its odor was similar to methyl benzoate. $n_D^{20} = 1.5190$. Lit. $n_D^{16} = 1.5181$. Hydrolysis gave benzoic acid, m.p. 121–121.5°; mixed with benzoic acid, m.p. 121–121.5°. The acid solution above was neutralized and extracted with ether. The ether layer was dried and alcoholic hydrogen chloride added; a precipitate formed (0.7 g.) which melted at 162–164°. After recrystallization from a mixture of ethanol, ethyl acetate, and isopropyl ether, it melted at 165–167°.

Anal. Calcd. for $C_{17}H_{22}NCl$: Cl, 12.85. Found: Cl, 12.73.

A mixed melting point with this compound and that prepared below showed no depression.

3-Dimethylamino-1,1-diphenylpropane. This was prepared by the treatment of 4-dimethylamino-2,2-diphenylbutanenitrile with sodium in isopropyl alcohol;[5] hydrochloride, m.p. 167–169°; methiodide, m.p. 190–192°.

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Synthesis of Some Symmetrical Aliphatic Quaternary Ammonium Iodides

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As part of an investigation of the effect of ionic dimensions on electric conductance,[2] a series of aliphatic quaternary ammonium iodides has been prepared (Table I).

The principal quaternization procedure consisted in refluxing alcoholic solutions of primary or tertiary amines with the required alkyl iodides. In some instances, the reaction mixtures were maintained at a *p*H of approximately 9 by the periodic addition of ethanolic potassium hydroxide.

As the quaternary salts were to be used for conductivity studies, their purity was of critical importance. Anion impurities were detected by titration with aqueous silver nitrate using calomel and silver-silver chloride electrodes. The titration procedure was initially applied to the successive recrystallization liquors rather than to solutions of the recrystallized salts. This time-saving step was applicable as it was found that after repeated recrystallizations, no appreciable change in effect on ionic conductance of subsequent recrystallization liquors was noted. At this point the ultimate criterion of purity was established by titration of the quaternary salts in methanol after they had been subjected to further successive recrystallizations. If the conductance of samples from recrystallization to recrystallization differed by less than 5%, the salts were deemed sufficiently pure for the conductance work.

Repeated recrystallization of tetraoctylammonium iodide failed to provide a product having satisfactory ionic conductance properties or analytical characteristics. Subjecting tetrahexadecylammonium iodide to repeated recrystallizations finally gave a product, however, which showed no alteration in its ionic conductance from recrystallization to recrystallization, but which gave unsatisfactory analytical results.

Confirmation of the presence of a quaternary nitrogen atom in the latter compound was established by measurement of the change in its ionic conductance effected by silver hydroxide, as compared with similar measurements of authentic samples of a representative quaternary ammonium iodide, and representative secondary and tertiary amine hydroiodides.

EXPERIMENTAL

Melting points are uncorrected. Microanalyses are by the Microanalytical Laboratory, Department of Chemistry, University of California.

Materials. The alkyl iodides which were not commercially available were prepared by the methods of Hartman, Byers, and Dickey[3a] and Finkelstein.[3b] The tertiary amines were obtained commercially or prepared by known methods.[4a,b]

General Procedures. The molecular amounts of reactants and other reaction data appear in Table I.

A. A mixture of the amine and the corresponding alkyl iodide was refluxed in a suitable solvent. Refluxing was discontinued intermittently, followed by cooling the reaction mixture and removing the reaction product.

B. Procedure A was modified in the following manner. After refluxing the reaction mixture was cooled, adjusted to *p*H 9 with 5% ethanolic potassium hydroxide, followed by the addition of an equal volume of water. The product was filtered and washed with water and ether. The yield of tetraheptylammonium iodide was increased to 31.4 g. (73%) by the addition of 50 ml. of commercial absolute ethanol and 12.5 g. (0.055 mole) of heptyl iodide to the diluted alkaline reaction filtrate and refluxing for 72 hr.

C. Procedure B was modified by maintaining the reaction mixture at a *p*H of approximately 9 by the periodic addition of 5% ethanolic potassium hydroxide. After refluxing, an equal volume of water was added and the mixture cooled.

D. A mixture of the tertiary amine and the alkyl iodide was heated in an open flask at 80°, following the procedure of Vernon and Masterson.[5]

E. Following the procedure described by Girard and Forneau,[6] ammonia gas was bubbled through the liquefied

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(1) Taken from a dissertation submitted by Stuart P. Eriksen in partial fulfillment of the requirements for the Ph.D. degree in Pharmaceutical Chemistry, 1956.

(2) In preparation.

(3) (a) W. W. Hartman, J. R. Byers, and J. B. Dickey, in A. H. Blatt, *Org. Syntheses*, **Coll. Vol. II**, John Wiley and Sons, New York, N. Y., 1943, p. 322; (b) H. Finkelstein, *Ber.*, **43**, 1528 (1910).

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TABLE I

TETRAALKYLAMMONIUM IODIDES $R_4N^+I^-$

No.[a]	R	Time, hr.	Solvent, ml.[b]	Millimoles		M.P., °	Yield, %	Formula	Analyses, %			
									Nitrogen		Iodine	
				Amine[c]	RI				Calcd.	Found	Calcd.	Found
1A[d]	Hexyl	31	50	83	104	102–103	83	$C_{24}H_{52}NI$	2.91	2.89	26.35	26.10
2B	Heptyl	72	100	80	82	121–122	40	$C_{28}H_{60}NI$	2.61	2.51	23.60	23.80
3C	Octyl	96	200	84	271	127–128	30	$C_{32}H_{68}NI$	2.36	2.41 2.32	21.37	22.60 20.27
3D	Octyl	12	—	7.4	14.6	127–128	39	—	—	—	—	—
4A	Decyl	80	25	14	16	118–120	55	$C_{40}H_{84}NI$	1.98	1.98	17.98	17.71
4C	Decyl	48	200	85	280	118–120	38	—	—	—	—	—
5C	Dodecyl	96	200	65	200	116–117	38	$C_{48}H_{100}NI$	1.71	1.95	15.51	15.56
6C	Tetradecyl	96	100	80	339	114.5–115	36	$C_{56}H_{116}NI$	1.51	1.69	13.64	13.35
7E	Hexadecyl	96	50	29	17	110–111	15	$C_{64}H_{132}NI$	1.34	1.81	12.17	11.50

[a] Compounds 1 and 5 were recrystallized from ethanol-water; 4 from ethanol-water or ethyl acetate; 2 and 3 from ethyl acetate; 6 from ethanol; 7 from commercial absolute ethanol. [b] Reaction solvent for 1 and 6, ethanol; 2, 4A, and 4C, commercial absolute ethanol; 3C and 5, carbon dioxide-free commercial absolute ethanol; 7, benzene-ethanol 1:1. [c] Primary amines: 3C, 4C, 5C, 6C, and 7E. Tertiary amines: 1A, 2B, 3D, and 4A. [d] Letters refer to procedures.

alkyl iodide maintained at approximately 185°. The solid reaction mixture was first extracted with cold ether, followed by extraction with 100 ml. of boiling ether. On cooling the hot ether extract deposited 4 g. of crystalline solid; m.p. 79–80°. Girard and Forneau isolated a product melting at the same temperature which was claimed to be tetrahexadecylammonium iodide.

Evaporation of the combined cold ether extract and the filtrate from the hot ether extract gave 7.9 g. of crystalline residue; m.p. 42–43°. A mixture of 6.9 g. of this residue (0.029 mole, calculated on the basis of hexadecylamine; lit.,[7] m.p. 44–46°) and the alkyl iodide was refluxed in benzene-ethanol. After cooling, the resulting product was filtered and recrystallized.

A freshly prepared alcoholic paste of silver hydroxide was added to saturated ethanolic solutions of samples of the recrystallized product, tetrabutylammonium iodide, ditetradecylamine hydroiodide, and trioctylamine hydroiodide. The specific resistances increased on addition of the silver hydroxide by factors of 1.04, 1.18, 6.28, and 6.35, respectively. The two quaternary salts changed resistance only slightly, as there is no decrease in concentration of conducting species.

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Pyridine-1-oxides. VI. Synthesis of Some 3-Styrylpyridine-1-oxides[1]

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During the course of an investigation of the chemistry of simple pyridine-1-oxides, it was found that 4-nitro-3-picoline-1-oxide condensed readily with benzaldehyde in ethanol or pyridine solution, in the presence of piperidine, to give 4-nitro-3-styrylpyridine-1-oxide.[2] Preliminary pharmacological screening of this compound indicated a high degree of antibacterial and antibiotic activity *in vitro*, and these findings prompted us to prepare a number of related 1-oxide derivatives.

4-Nitro-3-picoline-1-oxide was condensed with a number of other aromatic aldehydes, and the products formed are listed in Table I. All condensations could be carried out either in ethanol or in pyridine, with piperidine as catalyst. As pharmacological testing of many of these derivatives was difficult because of water insolubility, sodium salts of the phenolic derivatives were also prepared.

Treatment of 4-nitro-3-picoline-1-oxide with cinnamaldehyde, formaldehyde or glyoxal gave red, resinous materials, but no isolable products could be obtained. Attempts to condense 4-nitro-3-picoline-1-oxide with *p*-nitrosodimethylaniline failed.

Treatment of 4-nitro-3-styrylpyridine-1-oxide with acetyl chloride yielded 4-chloro-3-styrylpyridine-1-oxide. The action of thiourea in ethanol solution then gave the expected thiouronium salt, which on alkaline hydrolysis gave 4-mercapto-3-styrylpyridine-1-oxide along with a small amount of bis(1-oxy-3-styryl-4-pyridyl) sulfide.

It has already been pointed out by Jerchel and Heck[2] that neither 3-picoline, 4-nitro-3-picoline, nor 3-picoline-1-oxide gives a styryl derivative with benzaldehyde, and that both the 4-nitro and the 1-oxide groupings are therefore necessary for activation of the 3-methyl group. However, the 1-oxide grouping does effectively reduce electron density at the 3-position of the pyridine ring, as is clearly indicated by the observations that 3-amino-

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[1] For the previous paper in this series, see E. C. Taylor and J. S. Driscoll, *J. Am. Chem. Soc.*, in press.

[2] Since this original observation was made (E. C. Taylor and A. J. Crovetti, Abstracts of Papers, 126th ACS Meeting, New York City, 1954, p. 24-N) the synthesis of 4-nitro-3-styrylpyridine-1-oxide has been reported (D. Jerchel and H. E. Heck, *Ann.*, 613, 171 (1958)).