[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF JOHN CARROLL UNIVERSITY]

THE PREPARATION OF CERTAIN QUATERNARY THENYL AMMONIUM HALIDES[1]

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Within the past twenty years quaternary ammonium compounds have established a prominent place in the field of antiseptics and germicides. Unlike most disinfectants, these compounds exhibit not only germicidal action but also detergent, surface active, and wetting properties.

TABLE I

N-ALKYL-N,N-DIMETHYLTHENYLAMMONIUM IODIDES

R′	REACTION TIME (HOURS)	YIELD, %	M.P., °C.	RECRYSTN. SOLVENT	FORMULA	ANALYSIS			
						Iodine		Nitrogen	
						Calc'd	Found	Calc'd	Found
Methyl	1	91	151–152	EtOH/EtOAc	$C_8H_{14}INS$	44.87	45.01	4.94	4.43
Ethyl	1	80	134–135	EtOH/EtOAc	$C_9H_{16}INS$	42.76	43.17	4.71	4.47
n-Propyl	4	48	124–126	EtOH/EtOAc	$C_{10}H_{18}INS$	40.83	40.95	4.50	4.28
n-Butyl	4	46	123–123.5	EtOH/EtOAc	$C_{11}H_{20}INS$	39.07	39.05	4.31	3.91
n-Amyl	8	94	128–129	EtOH/EtOAc	$C_{12}H_{22}INS$	37.46	36.99	4.10	4.46
n-Hexyl	8	86	118	EtOH/pet. E[a]	$C_{13}H_{24}INS$	35.98	35.51	3.96	4.29
n-Heptyl	8	70	77.5	EtOH/EtOAc	$C_{14}H_{26}INS$	34.52	34.71	3.81	3.70
n-Nonyl	8	50	132–134	EtOH/EtOAc	$C_{16}H_{30}INS$	32.09	32.19	3.54	3.44
n-Tetradecyl	16	85	56–57	EtOH/EtOAc	$C_{21}H_{40}INS$	27.26	27.35	3.01	3.15
n-Hexadecyl	6	90	73–73.5	EtOH/EtOAc	$C_{23}H_{44}INS$	25.71	25.43	2.84	2.71
n-Octadecyl	6	90	80–81	EtOH/EtOAc	$C_{25}H_{48}INS$	24.33	24.01	2.69	2.74

[a] Petroleum ether, b.p. 30–40°.

Domagk (1) recognized the antiseptic properties of alkyldimethylbenzylammonium chloride, and Weilmuenster and Jordan (2) demonstrated that replacement of the benzyl radical by the furfuryl group in a series of quaternary ammonium iodides gave compounds with bactericidal and lytic action. Since certain thiophene derivatives possess germicidal properties, the study of alkyldimethylthenylammonium halides was undertaken.

The thenylamines were prepared by the method of Leuckart (3), and were

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then reacted with alkyl halides as follows:

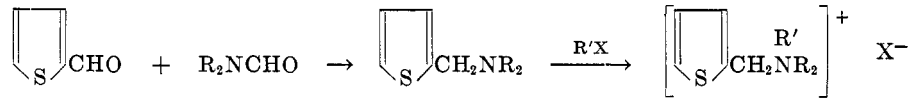

TABLE II

N-ALKYL-N,N-DIETHYLTHENYLAMMONIUM IODIDES

R′	REACTION TIME (HOURS)	YIELD, %	M.P., °C.	RECRYSTN. SOLVENT	FORMULA	ANALYSIS			
						Iodine		Nitrogen	
						Calc'd	Found	Calc'd	Found
Methyl	1	63	154	EtOH/EtOAc	$C_{10}H_{18}INS$	40.78	40.64	4.50	4.27
Ethyl	2	62	161	EtOH/EtOAc	$C_{11}H_{20}INS$	39.02	38.87	4.31	4.10
n-Propyl	10	54	149–151	EtOH/EtOAc	$C_{12}H_{22}INS$	37.41	36.92	4.12	3.84
n-Butyl	12	52	142–143	EtOH/i-PrOH	$C_{13}H_{24}INS$	35.92	35.65	3.96	3.75
n-Amyl	18	39	99–101	EtOH/i-PrOH	$C_{14}H_{26}INS$	34.55	34.83	3.81	3.57
n-Tetradecyl	5	24	11–12	EtOH/i-PrOH	$C_{23}H_{44}INS$	25.71	25.20	2.84	1.98
n-Hexadecyl	5	26	26	EtOH/i-PrOH	$C_{25}H_{48}INS$	24.33	23.69	2.67	2.36
n-Octadecyl	4	43	34–35	EtOH/i-PrOH	$C_{27}H_{52}INS$	23.09	22.63	2.55	2.61

EXPERIMENTAL

N,N-Dimethylthenylamine. A saturated solution containing 82 g. (1 mole) of dimethylamine hydrochloride was added dropwise to an excess of solid potassium hydroxide in a sidearm flask. The liberated base was bubbled through 51 g. (1 mole) of formic acid solution with constant stirring. After evaporating most of the water present in the mixture, 22.4 g. (0.2 mole) of 2-thiophene aldehyde (from Arapahoe Chemical Co.) was added to the crude dimethylformamide. After refluxing the reaction mixture for four hours, 200 ml. of water was added, the solution was made strongly alkaline, and the N,N-dimethylthenylamine was then steam-distilled, extracted with ether, and fractionated, the 165–169° portion being used for the preparation of salts.

Preparation of the quaternary ammonium salts. In precipitating the salts, 0.02 mole of the alkyl iodide was added to a benzene solution containing 0.02 mole of the amine, and the mixture was poured into a glass tube. The tube was then placed in a constant temperature bath adjusted to 70° for a period of 1 to 18 hours. The colorless crystals were separated, washed with benzene, and recrystallized, in most cases, by dissolving in hot absolute alcohol and reprecipitating by the addition of anhydrous ethyl acetate. Salts of the higher molecular weight halides are difficult to crystallize.

N,N-Diethylthenylamine and its salts were prepared in a similar manner.

SUMMARY

1. N,N-Dimethylthenylamine and N,N-diethylthenylamine have been prepared by the Leuckart (3) synthesis. N,N-Dimethylthenylamine and its methiodide had been prepared previously by another method (4).

2. A series of N,N-dimethylalkylthenylammonium iodides and N,N-diethylalkylthenylammonium iodides have been prepared.

3. Several similar ammonium bromides were also prepared, but were not obtainable in pure crystalline form.

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REFERENCES

(1) DOMAGK, *Deut. med. Wochschr.*, **61**, 829 (1935).
(2) WEILMUENSTER AND JORDAN, *J. Am. Chem. Soc.*, **67**, 415 (1945).
(3) LEUCKART AND JANSSEN, *Ber.*, **22**, 1409 (1889).
(4) HARTOUGH, *et al.*, *J. Am. Chem. Soc.*, **70**, 4015 (1948).