Both the 1,1- and 1,2-dichlorohexafluoropropanes have been prepared by Henne and Waalkes.[4,5]

In our work the 1,3-dichloride was made by first adding hydrogen fluoride to 1,2-dichloro-2-propene to form the difluoromonochloride, then chlorinating this to the hexachlorodifluoride and finally fluorinating the latter to the hexafluorodichloride.

Experimental

Preparation of CH_3–CF_2–CH_2Cl.—The procedure used was similar to that of Henne and Haeckl[6] with the important exceptions that the temperature was kept at 100°, by means of a steam-bath, instead of at 50–60° and that hydrogen chloride was bled off at a pressure of 270 lb. per sq. in. gage. This process resulted in a 60% yield of difluorochloride.

Preparation of CCl_3–CF_2–CCl_3.—Ten moles (1145 g.) of CH_3–CF_2–CH_2Cl was chlorinated in sunlight at 75–85° until the theoretical weight of chlorine had been absorbed. The crude material was fractionated to give a practically quantitative yield of CCl_3–CF_2–CCl_3, boiling range 193–195°.[7]

Preparation of CF_2Cl–CF_2–CF_2Cl.—In a steel pressure cylinder eight moles (1430 g.) of antimony trifluoride was treated with four moles (284 g.) of chlorine. Four moles (1147 g.) of CCl_3–CF_2–CCl_3 was added and the mixture was heated in an oil-bath at 210° for one hour, 230° for four hours and 250° during two hours. The pressure eventually rose to 300 lb. per sq. in. gage. The organic material was distilled from the cylinder, washed with concd. hydrochloric acid, neutralized and fractionated. There were obtained 370 g. of CF_2Cl–CF_2–CF_2Cl, b.p. 35.8°, $n^{20}D$ 1.3030, d^{20}_4 1.5730[8] and 300 g. of $CFCl_2$–CF_2–CF_2Cl intermediate, which can be converted to the above hexafluorodichloride.

Acknowledgment.—Part of the funds for this project was made available by the University of South Carolina Research Committee.

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(5) A. L. Henne and T. P. Waalkes, *ibid.*, **68**, 496 (1946).
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(8) Young and Murray[3] found the freezing range of this compound to be −126.3 to −125.4°.

DIVISION OF CHEMICAL ENGINEERING
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Some Quaternary Salts of 8-Hydroxyquinoline[1]

BY CARL T. BAHNER, LLOYD A. WALKER, FRANCES PIERCE AND EMMA KITE

The preparation of quaternary salts of substituted quinolines[2] has been extended to include salts of 8-hydroxyquinoline.

The salts were prepared by heating a mixture of the base and the appropriate organic halide at 100°, dissolving the resulting dark amorphous mass in hot alcohol, and adding ethyl acetate, ethyl ether or petroleum ether to throw out crystals of the product which was then recrystallized to a constant melting point before analysis. A 30-minute reaction period sufficed for the phenacyl bromides, but β-phenylethyl iodide required 48 hours and β-cyclohexylethyl bromide did not react satisfactorily even when heated 96 hours. The products were yellow, crystalline solids which were not readily soluble in water. The melting points and analytical data are shown in Table I.

Acknowledgments.—We wish to express our appreciation to Dr. M. J. Shear and Dr. J. L. Hartwell of the National Cancer Institute for arranging to screen these compounds against tumors in mice, and to Mr. George Biggerstaff and Mr. Lilburn Norton for assisting in the purification and analysis of one of these products.

TABLE I

8-HYDROXYQUINOLINIUM SALTS

Salt of 8-hydroxyquinoline with:	Empirical formula	M.p., °C.	Yield, %[a]	Analyses, % ionic halogen Calcd.	Found[b]
β-Phenylethyl iodide	$C_{17}H_{16}INO$	168.5–169[c]	85	33.64	33.46
Phenacyl bromide	$C_{17}H_{14}BrNO_2$	234–235	58	23.21	22.98
p-Methylphenacyl bromide	$C_{18}H_{16}BrNO_2$	223.5–224	46	22.26	22.09
p-Bromophenacyl bromide	$C_{17}H_{13}Br_2NO_2$	244.5–245	50	18.89	18.78
p-Iodophenacyl bromide	$C_{17}H_{13}BrINO_2$	257–258	58	16.99	16.68
p-Methoxyphenacyl bromide	$C_{17}H_{16}BrNO_3$	230	10	21.35	21.19
β-Naphthacyl bromide	$C_{21}H_{16}BrNO_2$	234–235	42[d]	20.02	19.93

[a] Crude yield of crystalline material unless otherwise indicated. [b] Average of two Volhard analyses for ionic halogen. [c] After final recrystallization from acetic acid. [d] Yield of pure material.

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Morpholinium Salts[1]

BY CARL T. BAHNER, EMMA KITE, FRANCES PIERCE, LYDIA MOORE RIVES, MADGE DEEL PICKENS AND CLIFFORD MYERS

In extending the study of analogs of quaternary pyridinium salts as possible anti-cancer agents[2] we have synthesized tertiary amine hydrohalides and quaternary ammonium salts containing a morpholine ring. Lutz and his associates[3] have prepared a number of N-substituted morpholines for use as intermediates or for testing as anti-malarials and Hazard, Corteggiani and Renard[4] have reported that 4-methyl-4-(2-phenylethyl)-morpholinium iodide produced marked hypertension in dogs at a dose of 5 mg./kg.

The tertiary amine hydrohalides were obtained by reaction of morpholine with the appropriate organic halide in equimolecular proportions and the quaternary salts were prepared from N-substituted morpholines in the same manner. The time required for reaction varied from a few minutes to a

(1) This investigation was supported in part by a research grant from the National Cancer Institute, of the National Institutes of Health, Public Health Service, for which we are grateful.
(2) *Cf.*, C. T. Bahner, M. Fielden, L. M. Rives and M. D. Pickens, THIS JOURNAL, **73**, in press (1951).
(3) Robert E. Lutz, Rufus K. Allison, Gilbert Ashburn, Philip S. Bailey, Marion T. Clark, John F. Codington, Adolf J. Deinet, James A. Freek, Robert H. Jordan, Norman H. Leake, Tellis A. Martin, Kent C. Nicodemus, Russell J. Rowlett, Jr., Newton H. Shearer, Jr., J. Doyle Smith and James W. Wilson, III, *J. Org. Chem.*, **12**, 617 (1947).
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(2) C. T. Bahner, W. K. Easley, M. D. Pickens, H. D. Lyons, L. L. Norton, B. G. Walden and G. Biggerstaff, THIS JOURNAL, **73**, 3499 (1951).

few days. 3,4-Dichlorophenacyl bromide reacted especially rapidly. The products were white or cream colored solids most of which were hygroscopic, even to the point of making analysis difficult, and readily soluble in water, but a few, such as the 3,4-dichlorophenacyl bromide, *p*-phenylphenacyl bromide, *p*-phenoxyphenacyl bromide and 5,6,7,8-tetrahydro-β-naphthacyl iodide salts of 4-methylmorpholine, were sparingly soluble in water. The *p*-alkylphenacyl bromide salts of 4-methylmorpholine were soluble in chloroform. The melting points and analytical data on the compounds are shown in Table I. Results of screening tests are to be reported elsewhere.

TABLE I

MORPHOLINE DERIVATIVES

Product from morpholine and	Empirical formula	Yield, %[a]	M.p., °C.[b]	Analyses, % Ionic halogen Calcd.	Found[c]
Phenylethyl bromide	$C_{12}H_{15}BrNO$	30	185–187	29.36	29.35
Phenylethyl iodide	$C_{12}H_{15}INO$	30	225–228	39.76	39.58
Phenacyl bromide	$C_{12}H_{16}BrNO_2$	80	230–233	27.93	28.03
p-Methylphenacyl bromide	$C_{13}H_{18}BrNO_2$	45	200–202	26.62	26.63
p-Bromophenacyl bromide	$C_{12}H_{15}Br_2NO_2$	..	242–244	21.89	21.78
p-Methoxyphenacyl bromide	$C_{13}H_{18}BrNO_3$	55	205–208	25.27	25.27
β-Naphthacyl bromide	$C_{16}H_{18}BrNO_2$	..	252–255	23.79	23.67
N-Methylmorpholine and					
Ethylene dibromide	$C_7H_{15}Br_2NO$	71	221	27.65	27.80
Cyclohexylethyl bromide	$C_{13}H_{26}BrNO$	..	242	27.49	27.56
Phenacyl bromide	$C_{13}H_{18}BrNO_2$	90	205–206	26.62	26.54[d]
p-Methylphenacyl bromide	$C_{14}H_{20}BrNO_2$	75	205-206.5	25.43	25.43
p-Ethylphenacyl bromide	$C_{15}H_{22}BrNO_2$	60[e]	159–160	24.55	24.52
p-Isopropylphenacyl bromide	$C_{16}H_{24}BrNO_2$	19[e]	165–166	23.35	23.58
p-*t*-Butylphenacyl bromide	$C_{17}H_{26}BrNO_2$	27[e]	189–190	22.43	22.40
p-Fluorophenacyl bromide	$C_{12}H_{17}BrFNO_2$	73	222	25.13	25.01
p-Chlorophenacyl bromide	$C_{12}H_{17}BrClNO_2$	64	245	23.9	23.9
p-Bromophenacyl bromide	$C_{13}H_{17}Br_2NO_2$	73	260	21.09	21.00
p-Iodophenacyl bromide	$C_{13}H_{17}BrINO_2$	85	247–249	18.75	18.78
3,4-Dichlorophenacyl bromide	$C_{13}H_{16}BrCl_2NO_2$	73[e]	250	21.65	21.51
m-Nitrophenacyl bromide	$C_{13}H_{17}BrN_2O_4$	70	177–178	23.16	23.08
p-Methoxyphenacyl bromide	$C_{14}H_{20}BrNO_3$	65	222–225	24.20	24.21
p-Phenylphenacyl bromide	$C_{19}H_{22}BrNO_2$	45[e]	202–203	21.24	21.15
p-Phenoxyphenacyl bromide	$C_{19}H_{22}BrNO_3$	20[e]	213–214	20.37	20.32
β-Naphthacyl bromide	$C_{17}H_{20}BrNO_2$	35[e]	205–206	22.82	22.53
α-Bromo-1-propionaphthone	$C_{13}H_{22}BrNO_2$	36[e]	209–210	21.95	21.79
5,6,7,8-Tetrahydro-β-naphthacyl iodide	$C_{17}H_{24}INO_2$	23[e]	192–193	31.63	31.73
2-(α-Bromoacetyl)-thiophene	$C_{11}H_{16}BrNO_2S$	18[e]	217–218	26.10	25.84
4,4′-Bis-(bromoacetylphenyl) ether, (bis salt)	$C_{26}H_{34}Br_2N_2O_5$	21[e]	219–220	26.02	25.93
N-(2-Hydroxyethyl)-morpholine and					
α-Naphthacyl bromide	$C_{18}H_{22}BrNO_3$	20[e]	183–184	21.01	20.96
β-Naphthacyl bromide	$C_{18}H_{22}BrNO_3$	34[e]	205–206	21.01	20.86
4-Fluoro-α-naphthacyl bromide	$C_{18}H_{21}BrFNO_3$	14[e]	208–209	20.06	19.78
2-(α-Bromoacetyl)-thiophene	$C_{12}H_{18}BrNO_3S$	39[e]	212	23.77	23.56
N-Phenylmorphloine and					
Phenacyl bromide	$C_{18}H_{20}BrNO_2$	85	150–151	21.86	22.03
N-Phenylethylmorpholine and					
Methyl iodide	$C_{13}H_{20}INO$	50	185-187	38.09	37.99
Allyl bromide	$C_{16}H_{22}BrNO\cdot{}^1/_2H_2O$	32	154	24.88	24.82[f]
Benzyl bromide	$C_{19}H_{24}BrNO\cdot{}^1/_2H_2O$	35	190–192	21.52	21.73[g]
Phenacyl bromide	$C_{20}H_{24}BrNO_2$	50	167.5–168.0	20.48	20.45
m-Nitrophenacyl bromide	$C_{20}H_{23}BrN_2O_4$	30	161–162	17.95	17.94
p-Ethoxyphenacyl bromide	$C_{22}H_{28}BrNO_3\cdot 1^1/_2H_2O$	72	182–183	17.36	17.07[h]
p-Phenylphenacyl bromide	$C_{26}H_{28}BrNO_2$	60	209–211	17.13	16.92
β-Naphthacyl bromide	$C_{24}H_{26}BrNO_2\cdot{}^1/_2H_2O$	50	178	17.71	17.59[i]
α-Phenyl-β-(4-morpholinyl)-ethanol and					
Methyl iodide	$C_{13}H_{20}INO_2$	98	147	36.35	36.23

[a] Crude yield of crystalline material unless otherwise indicated. [b] Compounds melted with decomposition. [c] Average of two Volhard analyses unless otherwise indicated. [d] Calcd.: C, 52.00; H, 6.04. Found: C, 51.99; H, 6.11. [e] Yield of fully purified material. [f] Calcd.: C, 56.03; H, 7.16; N, 4.36. Found: C, 56.48; H, 7.09; N, 4.29. [g] Calcd.: C, 61.39; H, 6.73; N, 3.77. Found: C, 61.88; H, 6.69; N, 3.85. [h] Calcd.: C, 57.35; H, 6.73; N, 3.04. Found: C, 57.10; H, 6.23; N, 2.94. [i] Calcd.: C, 64.13; H, 6.06; N, 3.12. Found: C, 64.14; H, 6.08; N, 3.03.

The methods of preparation are illustrated by the following examples.

4-(*p*-Methylphenacyl)-morpholine Hydrobromide.—Heat was evolved when 3.5 g. of morpholine and 5.4 g. *p*-methylphenacyl bromide were mixed without any solvent. The reddish-brown sticky paste recrystallized from ethanol yielded 5.35 g. (45%) of white crystals, m.p. 200–202°.

4-Methyl-4-(5,6,7,8-tetrahydro-β-naphthacyl)-morpholinium Iodide.—5,6,7,8-Tetrahydro-β-naphthacyl bromide was prepared in 43% yield by dropwise addition of a mixture of 204 g. of bromoacetyl bromide (1.01 moles) and 120 g. of tetralin (0.91 mole) in 600 ml. of carbon disulfide to 150 g. of aluminum chloride (1.13 moles) in 1200 ml. of carbon disulfide at 0–10°, stirring 2 hours, and decomposing with ice and dilute hydrochloric acid, m.p. 69° after recrystallization from isopropyl alcohol to constant melting point. This product was also obtained in approximately the same yield by bromination of 5,6,7,8-tetrahydro-2-acetonaphthone in acetic acid. Thirty grams of the bromide dissolved in 150 ml. of acetone, mixed with 25 g. of sodium iodide, the sodium bromide filtered off, the acetone solution evaporated and the residue recrystallized from hot methanol yielded 18 g. (49%) of 5,6,7,8-tetrahydro-β-naphthacyl iodide, m.p. 58–59°. A mixture of 7.80 g. of this iodide (0.026 mole) and 2.36 g. of 4-methylmorpholine (0.026 mole) in 50 ml. of chloroform produced a large quantity of white crystals within 36 hours. After standing several days the salt was filtered off and purified by repeatedly dissolving in hot methanol and adding ether until a constant melting point of 192–193° was reached; yield of pure product 2.38 g. (23%).

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Oximes of β-Naphthacyl Halides and their Pyridinium Salts[1]

BY CARL T. BAHNER, PAUL T. SCOTT, CAROLYN CATE, BETTY GAY WALDEN AND H. DAVID BALDRIDGE, JR.

An oxime of β-naphthacylpyridinium iodide has been reported to damage sarcoma cells *in vivo*,[2] but the configuration of the oxime was not specified. In order to settle this point we have prepared the antiform of the oximes of β-naphthacyl bromide and iodide and their pyridinium salts and have submitted samples of the salts to the National Cancer Institute for screening. The 3-bromopyridinium salt has been reported in another article.[3]

Experimental

Anti-β-naphthacyl Bromide Oxime (I).—A saturated solution of 13.95 g. of hydroxylamine hydrochloride in water was added to 50 g. of β-naphthacyl bromide in 1800 ml. of methanol at room temperature, the mixture allowed to stand 6 hours at room temperature, a part of the methanol removed by vacuum distillation, the liquid cooled and filtered to recover one crop of crystals, the removal of solvent and chilling repeated to obtain a second and a third crop of crystals which were then subjected to systematic fractional crystallization from methanol. There were obtained 15.4 g. of crystals melting at 172.5°, 9.30 g. melting at 170° and 8.0 g. melting at 169°. Repeated recrystallization produced a fraction melting at 174°. A sample of the less soluble, high melting crystals was subjected to Beckmann rearrangement followed by hydrolysis and a 61% yield of β-naphthylamine was isolated, but no β-naphthoic acid could be detected.

Anti-β-naphthacylpyridinium Bromide Oxime.—The pyridinium salt, white crystals, m.p. 245°, was obtained in 83% yield by reaction of I with pyridine in alcohol. It was purified by recrystallization from ethanol and water.

Anal. Calcd. for $C_{17}H_{15}BrN_2O$: Br, 23.25. Found: Br, 23.21, 23.31.

Anti-β-naphthacyl Iodide Oxime (II).—A solution of 0.92 g. of I dissolved in a minimum volume of acetone was mixed with 1.42 g. (excess) of sodium iodide in 10 ml. of acetone, the sodium bromide removed after several hours by filtration and the oxime obtained in crystalline form by cooling the solution in an ice-bath and filtering. After repeated recrystallization from ethanol the product melted at 148°. Beckmann rearrangement, followed by hydrolysis, gave a 71% yield of β-naphthylamine, m.p. 105–107°. A portion of this compound was treated with acetic anhydride to give the N-acetyl derivative, m.p. 134–135°. No β-naphthoic acid was isolated.

The oximes appeared to be stable for several days at room temperature, but after several weeks most of the samples had turned brown and showed other indications of decomposition.

Anti-β-naphthacylpyridinium Iodide Oxime.—A mixture of 2.5 g. of II (0.008 mole) and 0.63 g. of pyridine (0.008 mole) in a little acetone seemed to react completely within a few minutes. After several hours 2.6 g. of white crystals were removed by filtration and washed with chloroform; m.p. 222–223° (dec.) after recrystallization from methanol.

Anal. Calcd. for $C_{17}H_{15}IN_2O$: C, 52.34; H, 3.88. Found: C, 51.94; H, 4.02.

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DEPARTMENT OF CHEMISTRY
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Investigations in the Acetylene Series. I. The Reactions of 3-Methyl-1-butyn-3-ol with Phosphorus Trichloride and of 3-Methyl-3-buten-1-yne with Hydrochloric Acid

BY ERNST D. BERGMANN AND D. HERRMAN

Hennion, Sheehan and Maloney[1] have recently reported on the reaction of 3-methyl-1-butyn-3-ol (I) with hydrochloric acid under various conditions. The present note supplements their conclusions.

In the reaction of 3-methyl-1-butyn-3-ol (I) with phosphorus trichloride, the corresponding *t*-chloride (II) and 3-methyl-1-chloro-1,3-butadiene (V) were obtained; they were identified by their reactions. When hydrochloric acid reacted upon (I), 3-methyl-1-chloro-1,2-butadiene (VII), isolated by Hennion and co-workers[1] in their experiments,

(1) This investigation was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, Public Health Service, for which we are grateful.

(2) Albert J. Dalton, in "Approaches to Cancer Chemotherapy," American Association for the Advancement of Science, F. R. Moulton, Editor, Washington, D. C., 1947, p. 246; *cf.* J. L. Hartwell and S. R. L. Kornberg, THIS JOURNAL, **68**, 1131 (1946).

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