move the catalyst and the filtrate was poured into 50 ml. of a 10% HCl solution, with stirring. The precipitated hydrochloride of dicyclohexylamine was filtered onto a Büchner funnel and washed several times with 25-ml. portions of distilled water. The material from the Büchner funnel was removed and placed into 100 ml. of a 15% solution of NaOH, with stirring. This mixture was cooled and extracted with four 50-ml. portions of ethyl ether. After flash-distilling the ethyl ether, the fraction boiling from 256–257° at atmospheric pressure was collected. Infrared spectrograms of the radioactive material compared to that of a freshly distilled sample of dicyclohexylamine (b.p. 256–257°) at atmospheric pressure) established the identity of the synthesized material and also that it was of a high degree of purity.

SYNTHESIS OF DICYCLOHEXYLAMMONIUM-1-1′-C^{14} NITRITE (Reference 2)

The dicyclohexylamine-1-1′-C^{14} (1.00 g.) was added to 8 ml. of distilled water containing 0.2 ml. of 85% phosphoric acid, and 0.40 g. of sodium nitrite was added at 0°, with stirring. The dicyclohexylammonium-1-1′-C^{14} nitrite precipitated and was filtered onto a Büchner funnel, washed with a 2-ml. portion of cold water, and dried. The material was placed into twice its weight of cold water, and the mixture was stirred. The purified dicyclohexylammonium-1-1′-C^{14} nitrite then was filtered onto a Büchner funnel, washed with a 2-ml. portion of cold water, and dried.

The synthesized material had an activity of 62 microcuries. Thus the radiochemical yield of dicyclohexylammonium-1-1′-C^{14} nitrite was 31%. The material had a melting point of 153.0–154.5° with decomposition. (Literature[3] m.p. 154.5°.)

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The opinions or assertions contained herein are the private ones of the writer, and are not to be construed as official or reflecting the views of the Navy Department, or the Naval service at large.

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(2) U. S. Patent 2,544,245 assigned to Shell Development Company (Preparation of dicyclohexylammonium nitrite).

(3) *Dicyclohexylammonium Nitrite*, A. Wachter, T. Skei, and N. Stillman, Shell Development Company, presented at the symposium on Industrial Use of Corrosion Inhibitors, March 1951, Conference, New York National Association of Corrosion Engineers.

2-N-Alkylaminopyrimidine

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It has been previously reported that 2-aminopyrimidine methiodide warmed with an ethanolic or aqueous solution of sodium hydroxide yields 2-N-methylaminopyrimidine.[2,3] Treatment of the methiodide with a cold aqueous solution of sodium hydroxide has been reported to give 1-methyl-2-iminopyrimidine.[3] Prior to this recent disclosure, it was desirable to determine the alkylation products when 2-aminopyrimidine was treated with ethyl or *n*-butyl iodide. Our results indicate that the major product in both cases is the 2-N-alkylaminopyrimidine and that the 1-N-alkyl products, if formed, are very unstable in dilute sodium hydroxide in the cold. These compounds were synthesized by (A) reaction of 2-chloropyrimidine with ethyl or *n*-butylamine for comparison purposes and (B) reaction of 2-aminopyrimidine with ethyl or *n*-butyl iodide followed by neutralization with cold aqueous sodium hydroxide.

EXPERIMENTAL[4]

2-Chloropyrimidine. The compound was prepared from 2-aminopyrimidine[5] as described by Overberger, Kogon, and Minin,[6] m.p. 64–65°.

Preparation of 2-N-ethylaminopyrimidine. Method A. From 2-chloropyrimidine and ethylamine. A solution of 11.4 g. (0.1 mole) of 2-chloropyrimidine, 9.5 g. (0.21 mole) of ethylamine, and 50 ml. of absolute alcohol was refluxed for 4 hours. The solution was cooled in an ice-bath for one hour. The ethylamine hydrochloride that precipitated was filtered and washed with ether, 7.33 g. (95.5%), m.p. 107–108°. The filtrate was evaporated on a steam-bath and the residue was recrystallized from petroleum ether (b.p. 30–60°), yield 11.0 g. (89.6%), m.p. 50–51°.

Anal. Calc'd for $C_8H_9N_3$: C, 58.5; H, 7.3; N, 34.1. Found: C, 58.7; H, 7.6; N, 34.5.

The *picrate* was prepared by adding an excess of a saturated solution of ethereal picric acid to an ethereal solution of the free base. A yellow crystalline solid precipitated which was recrystallized from ethyl alcohol, m.p. 160–161°.

Anal. Calc'd for $C_{12}H_{12}N_6O_6$: N, 23.8. Found: N, 23.6.

Method B. From 2-aminopyrimidine and ethyl iodide. A mixture of 9.4 g. (0.1 mole) of 2-aminopyrimidine, 31.2 g. (0.2 mole) of ethyl iodide, and 75 ml. of absolute alcohol was refluxed for 24 hours. The resulting solution was concentrated to half the volume and was chilled in an ice-bath for one hour. The iodide (I) that precipitated was filtered and washed thoroughly with ether, 21.5 g. (86.0%). Compound I was recrystallized from ethyl alcohol yielding 21.0 g. (84.0%) of a white crystalline solid, m.p. 154–155°.

Anal. Calc'd for $C_6H_{10}IN_3$: C, 28.7; H, 4.0; N, 16.8. Found: C, 28.4; H, 3.9; N, 16.8.

The free base was obtained by the addition of sufficient cold (10°) aqueous sodium hydroxide solution to neutralize a cold (10°) aqueous solution of compound I. The aqueous solution was extracted with three 25-ml. portions of ether, and the ether then was dried over sodium sulfate for 24 hours. After the removal of the drying agent, the solvent was removed on a steam-bath and the residue was recrystallized from petroleum ether (b.p. 30–60°). The product, 8.5 g.

(1) Present address: Jackson Laboratory, Organic Chemicals Department, E. I. du Pont de Nemours & Co., Deepwater, New Jersey.

(2) Overberger and Kogon, *J. Am. Chem. Soc.*, **76**, 1065 (1954).

(3) Brown, Hoerger, and Mason, *J. Chem. Soc.*, 4035 (1955).

(4) All melting points are uncorrected.

(5) A sample of 2-aminopyrimidine was generously contributed by the American Cyanamid Company.

(6) Overberger, Kogon, and Minin, *Org. Syntheses*, **35**, 35 (1955).

(85%), melted at 50–51°. A mixture melting point with a sample of 2-N-ethylaminopyrimidine prepared by procedure *A* gave no depression, m.p. 50–51°. The picrate prepared from ethereal picric acid and recrystallized from ethyl alcohol melted at 160–161°. A mixture melting point with the picrate prepared from procedure *A* gave no depression, m.p. 159–160°.

Preparation of 2-N-ethylaminopyrimidine picrate from I. To 2.5 g. (0.01 mole) of I dissolved in 5 ml. of ethyl alcohol was added an excess of ethereal picric acid. A yellow crystalline solid precipitated immediately. The picrate was filtered and recrystallized from ethyl alcohol, 3.17 g. 90.0%), m.p. 160–161°. A mixture melting point with 2-N-ethylaminopyrimidine picrate, m.p. 160–161°, prepared from procedure *A* gave no depression, m.p. 160–161°.

Preparation of 2-N-n-butylaminopyrimidine. This compound was prepared by procedure *A* and *B* given for 2-N-ethylaminopyrimidine. The iodide (II) recrystallized from ethyl alcohol was obtained in 55.0% yield and melted at 144–146°.

Anal. Calc'd for $C_8H_{14}IN_3$: C, 34.4; H, 5.0; N, 15.1. Found: C, 34.1; H, 5.2; N, 15.0.

The *free base* was obtained from II in 87% yield, b.p. 75–80° (2 mm.), n_D^{20} 1.5328, and by the reaction of 2-chloropyrimidine with *n*-butylamine in 69.0% yield, b.p. 76–78° (2 mm.), n_D^{20} 1.5330.

Anal. Calc'd for $C_8H_{13}N_3$: C, 63.5; H, 8.6; N, 27.8. Found: C, 63.4; H, 8.4; N, 27.5.

The *picrate* prepared from the free base and II respectively was recrystallized from ethyl alcohol and melted at 126–127°, (128–129°).[7]

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(7) Behnisch and Mietzsch, German Patent 889,445, September 10, 1953 (*Chem. Abstr.*, **48**, 12813[e]). The *picrate* was prepared from the condensation product of propargylaldehyde with *n*-butylguanidine sulfate.

N-Substituted 1-, 2-, and 4-Aminofluorene Derivatives[1]

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The procedure for the preparation of 1-aminofluorene usually involves 6 steps starting with fluoranthene.[4,5] In attempting to prepare a large quantity of 1-aminofluorene for cancer research studies it was found that the reduction of 1-fluorenonecarboxylic acid to 1-fluorenecarboxylic acid was the weak link in the synthesis. In our hands difficult-to-purify mixtures and unsatisfactory yields resulted when attempts were made to prepare large quantities of 1-fluorenecarboxylic acid by hydrazine,[4] sodium amalgam,[6] or zinc amalgam reduction.[7] Dissatisfaction with the reduction procedure has also been expressed by Gutmann and Albrecht.[8] Ring-reduced by-products were obtained in the sodium amalgam reduction and 3-hydroxy-1,2-diazofluoranthene[9] was isolated from the hydrazine reduction procedure.

A simplified 5-step preparation resulting in higher yields of 1-aminofluorene has been developed. This method depends on carrying out the reduction at a later stage in the synthesis. As each step has been repeated at least 8 times, the procedure is believed to be reliable. Essentially the sequence consists of fluoranthene → 1-(9-fluorenone)carbonyl azide → 1-acetylamino-9-fluorenone → 1-aminofluorene.

The effect of N-acyl groups on the biological properties of biologically important amines is worthy of more intensive study since 2-trifluoroacetylamino fluorene has been reported to be much more carcinogenic[10] to Buffalo rats than is the well-known 2-acetylaminofluorene.[11,12] For this reason N-substituted fluoroacetyl, difluoroacetyl, trifluoroacetyl, and perfluoropropionyl derivatives of the carcinogenic 2-aminofluorene[11,13] as well as of the 1- and 4-isomers were prepared. Included in Table I are other acyl derivatives and Schiff bases. 4-Aminofluorene was prepared by a six step procedure starting from phenanthrene.[14]

EXPERIMENTAL[15]

1-(9-Fluorenone)carbonyl azide. Reaction between 1-(9-fluorenone)carbonyl chloride, m.p. 130–131°, dissolved in acetone and sodium azide in water solution gave a 90% yield of crude product, dec. 86°. Lit. m.p. 90–91°.[16] Recrystallization from heptane gave a 62% yield of yellow needles, m.p. 148–150°. The infrared spectrum in chloroform had a very strong band at 4.88 μ which is apparently due to the azido group.

1-Acetylamino-9-fluorenone. A solution of 2.49 g. of dry 1-(9-fluorenone)carbonyl azide, m.p. 142–146°, in 33 ml. of acetic anhydride was refluxed for 4 hours and allowed to

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(3) Taken in part from a thesis to be presented by Barbara Chastain in partial fulfillment of the requirements for the M.S. Degree.

(4) Bergmann and Orchin, *J. Am. Chem. Soc.*, **71**, 1111 (1949).

(5) Weisburger and Weisburger, *J. Org. Chem.*, **18**, 864 (1953).

(6) Fieser and Seligman, *J. Am. Chem. Soc.*, **57**, 2174 (1935).

(7) Forrest and Tucker, *J. Chem. Soc.*, 1140 (1948).

(8) Gutmann and Albrecht, *J. Am. Chem. Soc.*, **77**, 175 (1955).

(9) Campbell and Stafford, *J. Chem. Soc.*, 299 (1952).

(10) Morris, *J. Natl. Cancer Inst.*, **15**, 1535 (1955).

(11) Wilson, DeEds, and Cox, *Cancer Research*, **1**, 595 (1941).

(12) Hartwell, *Survey of Compounds Which Have Been Tested for Carcinogenic Activity*, Fed. Sec. Agency, Washington, 1951.

(13) Morris, Dubnik, and Johnson, *J. Natl. Cancer Inst.*, **10**, 1201 (1950).

(14) Sawicki, Ray, and Glocklin, *J. Org. Chem.*, **21**, 243 (1956).

(15) Melting points are uncorrected. Analyses are by Peninsular ChemResearch, Inc., Gainesville, Florida.

(16) Cook and Moffatt, *J. Chem. Soc.*, 1160 (1950).