slowly due to the tendency for the mixture to froth. The epoxide was condensed in the ice-cooled trap and no material was condensed in the Dry Ice-cooled trap. The epoxide was then cooled in Dry Ice, the water which had been carried over from the aqueous solution was frozen out, the epoxide was decanted, dried and rectified. The yield was 12.5 g. (96%).

Ethyl α-Bromo-$\alpha,\gamma,\gamma,\gamma$-tetrafluoroacetoacetate.—Ethyl $\alpha,\gamma,\gamma,\gamma$-tetrafluoroacetoacetate (42 g.) was dissolved in carbon tetrachloride (150 ml.) and the mixture was heated to 70°. Bromine (40 g.) was added dropwise over a period of 12 hours and the mixture was then stirred and heated for an additional 12 hours. The carbon tetrachloride and a small amount of bromine was distilled out of the mixture, and the pressure was reduced to 15 mm., and distillation was continued. Ethyl α-bromo-$\alpha,\gamma,\gamma,\gamma$-tetrafluoroacetoacetate (50 g., 72%) was obtained boiling at 51–52° at 15 mm.

Hydrolysis of Ethyl α-Bromo-$\alpha,\gamma,\gamma,\gamma$-tetrafluoroacetoacetate.—A mixture of ethyl α-bromo-$\alpha,\gamma,\gamma,\gamma$-tetrafluoroacetoacetate (14 g.) and 50% sulfuric acid (100 ml.) was refluxed for 6 hours. The aqueous solution was then cooled and extracted with ether. The ether extract was dried with sodium sulfate and distilled. When the pot temperature reached 50°, the residue was mixed with 50 ml. of concd. sulfuric acid and distillation was continued. 3-Bromo-1,1,1,3-tetrafluoroacetone (9 g., 90%) was obtained boiling at 65–66°.

Hydrolysis and Bromination of Ethyl α-Bromo-$\alpha,\gamma,\gamma,\gamma$-tetrafluoroacetoacetate.—The ester (28 g.) and 50% sulfuric acid (150 ml.) were mixed in a 500-ml., 3-necked flask which was equipped with a reflux condenser, a sealed stirrer and an addition funnel. The mixture was heated to 90° and bromine (16 g.) was added dropwise. Heating and stirring was continued for an additional two hours and then the aqueous solution was cooled and extracted with ether. The ether extract was dried with anhydrous sodium sulfate and distilled. After distillation of the ether, the residue was mixed with concd. sulfuric acid (50 ml.) and distillation was continued. 3,3-Dibromo-1,1,1,3-tetrafluoroacetone (25 g., 83%) was obtained boiling at 81–82°.

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Reactivity of 5-Bromoisocytosine with Some Amines

BY ARTHUR P. PHILLIPS

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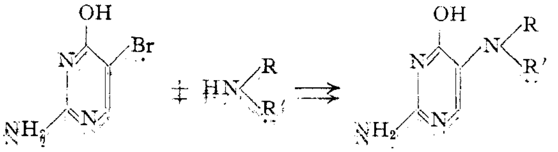
The reactivity of 5-bromouracil with amines permitted the preparation of a series of 5-substituted aminouracils for chemotherapeutic testing.[1] In order to obtain other 5-substituted aminopyrimidines bearing additional amino groups, the reactivity of 5-bromoisocytosine toward amines has now been examined.



The bromine of 5-bromoisocytosine is active for replacement reactions with amines but apparently less so than that of 5-bromouracil. Piperidine and morpholine reacted rapidly with 5-bromoisocytosine to give high yields of the 5-substituted amino derivatives. On the other hand, *n*-butylamine, ethylamine and methylbenzylamine either gave no reaction or no good product was isolated even when more strenuous reaction conditions were employed than were necessary to produce excellent yields with 5-bromouracil.

For example when a mixture of 0.1 mole of 5-bromouracil and 0.3 mole of *n*-butylamine was refluxed for three hours on a steam-bath a 90–100% yield of 5-*n*-butylaminouracil was obtained. But when 0.1 mole of 5-bromoisocytosine in 0.4 mole of *n*-butylamine was refluxed for 24 hours on the steam-bath a nearly quantitative recovery of unchanged 5-bromoisocytosine resulted.

Experimental

5-Piperidinoisocytosine.—A mixture of 19 g. (0.1 mole) of 5-bromoisocytosine and 25 cc. (21 g., 0.25 mole) of piperidine was refluxed in a metal-bath at 140–150° for four hours. The reaction mixture was washed out with 100 cc. of hot water and a little acetic acid was added bringing the *p*H to 8–8.5. After cooling, filtration gave 19 g. (100%) of white crystals. The product was purified by several reprecipitations from dilute hydrochloric acid solution by the addition of aqueous ammonia to *p*H 8 and then melted at 278–280°.

When 5-piperidinoisocytosine was treated with an excess of methanolic hydrogen chloride the dihydrochloride was formed. This salt was purified by several recrystallizations from methanol–ethyl acetate mixtures; m.p. 269–270° (dec.).

Anal. Calcd. for $C_9H_{16}Cl_2N_4O$: C, 40.4; H, 6.0. Found: C, 40.8; H, 5.8.

5-Morpholinoisocytosine.—A mixture of 19 g. (0.1 mole) of 5-bromoisocytosine and 25 cc. (22 g., 0.25 mole) of morpholine was refluxed in a metal-bath at 150–160° for four hours. The reaction product was taken up in about 80–90 cc. of hot water, the *p*H was adjusted to 6–7 with dilute acetic acid, and on cooling there was obtained 18 g. (90–95%) of white crystals. After recrystallization from hot water the product melted at 275–276° (dec.). The analytical sample was dried *in vacuo* at 120°.

Anal. Calcd. for $C_8H_{12}N_4O_2$: C, 48.9; H, 6.1. Found: C, 48.7; H, 6.1.

Attempted Reaction of *n*-Butylamine and 5-Bromoisocytosine.—A mixture of 19 g. (0.1 mole) of 5-bromoisocytosine and 35 cc. (25 g., 0.35 mole) of *n*-butylamine was refluxed on the steam-bath for 24 hours. The bulk of the *n*-butylamine was removed by evaporation. The residue was purified by reprecipitation from alkali solution by the addition of acid to *p*H 7–8. In this way 16–18 g. of solid was recovered which, upon purification both as the base and as the hydrochloride, was proved by analyses to be the original 5-bromoisocytosine. The recovery of unreacted bromo compound represents 85–95%.

Similar reactions were attempted with a number of other amines, ethylamine, methylbenzylamine, etc., but either the bromoisocytosine was recovered unchanged or no good product was readily isolable.

Acknowledgment.—The author is indebted to S. W. Blackman for the microanalyses included.

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The Preparation of Free Hydroxylamine and Deutero-hydroxylamine

BY R. E. NIGHTINGALE AND E. L. WAGNER

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During a study of the infrared spectrum of crystalline hydroxylamine,[1] it was felt that additional information was needed which might be provided by deutero-hydroxylamine. It is well known that

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[1] A. P. Phillips, THIS JOURNAL, **73**, 1061 (1951).

[1] R. E. Nightingale and E. L. Wagner, submitted to *J. Chem. Phys.*

spectra of isotopic molecules, particularly of deutero compounds when they are available, are valuable aids in the interpretation of infrared data.

The compound D_2NOD has not been reported in the literature. The usual method for the preparation of H_2NOH involves the neutralization of hydroxyammonium chloride by sodium butoxide in a hydrogen-rich solvent such as butanol.[2] This is obviously not suited for the preparation of D_2NOD using reasonable amounts of D_2O. Moreover, our attempts to make D_2NOD by successive exchanges of H_2NOH with D_2O have been unsuccessful. It appears that a stable hydrate is formed which makes it impossible to recover the exchange water from the mixture, H_2NOH–H_2O, by a vacuum distillation. Another method of preparation of D_2NOD was attempted and proved to be successful. Uhlenhuth,[3] in 1900, prepared free hydroxylamine by the thermal decomposition of tertiary hydroxylammonium phosphate at reduced pressure. We have prepared H_2NOH by a modification of this procedure, which, when followed by two or three fractional sublimations resulted in a product melting at 32–33°, the same as that ascribed to pure hydroxylamine. Infrared spectra of this material in the region 500–4000 cm.$^{-1}$ were identical with those of H_2NOH prepared in the usual manner.

This method was adapted to the preparation of D_2NOD. The salt $(H_3NOH)_3PO_4$ was first converted to $(D_3NOD)_3PO_4$ by exchange with heavy water and this was followed by thermal decomposition to D_2NOD. The material was collected in a tube in the vacuum system, fractionally sublimed, and finally sublimed onto the rocksalt sample support of an infrared low-temperature cell.[4] In addition to offering a simple method for the preparation of D_2NOD using small amounts of D_2O, this method also has some obvious advantages for the preparation of small amounts of H_2NOH. A sample may be prepared and used on the same day. The melting point may be checked easily in the vacuum system by subliming a small amount into a capillary tube. All transfers are carried out *in vacuo*, thereby eliminating the danger of reaction with atmospheric vapors. Finally, the material may be conveniently purified by fractional sublimation.

Experimental Procedure

$(H_3NOH)_3PO_4$ was prepared by precipitation from a hot solution of H_3NOHCl and Na_3PO_4. This was filtered and dried in a vacuum desiccator over H_2SO_4.

For the preparation of D_2NOD, 0.7 g. $(H_3NOH)_3PO_4$ was introduced into a flask on the vacuum line. Enough D_2O (5.5 ml.) was added to dissolve the salt at 80°. The mixture was evaporated to dryness at reduced pressure and room temperature. The system was brought back to atmospheric pressure with dry nitrogen and a second portion of D_2O was added. Three more exchanges were made and the salt was finally dried by pumping at 0.015 mm. for several hours followed by a final heating to 110–120° at 13 mm. pressure.

The distillation of the D_2NOD from the salt was carried out at 13 mm. and 135–150°. Heating was done with a glycerol-bath which could be removed rapidly if necessary, and was carried out with the protection of a safety glass explosion screen. A bleeder valve between the pump and the vacuum system was employed in order to add dry nitrogen to maintain the pressure at 13 mm. during distillation. Reaction began at about 130° at this pressure. The D_2NOD was collected in a portion of the apparatus at 0°. This material was fractionally sublimed into a tube at −80° and kept there until needed. Deutero-hydroxylamine prepared in this manner had a deuterium purity, as estimated from its infrared spectrum, of about 97%.

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The Melting Transition of Polymethylene[1]

BY L. MANDELKERN, M. HELLMANN, D. W. BROWN, D. E. ROBERTS AND F. A. QUINN, JR.

RECEIVED APRIL 14, 1953

Polymethylene, a linear polymeric hydrocarbon of high molecular weight, serves ideally as a model polymer in various physicochemical studies, because of the simplicity of its structure. It is particularly well suited for an investigation of the crystallization behavior of chain molecules, and in this connection we should like to present the results of a study of its volume–temperature behavior, and its melting temperature, T_m.

In Fig. 1, the relative volume of polymethylene (relative to that at 137°), as determined dilatometrically, is plotted as a function of temperature. A well defined first-order transition, or melting temperature, characterized by the disappearance of the last traces of crystallinity, occurs at 136.5 ± 0.5°, and 70% of the melting occurs in only a three to four degree interval. For comparative purposes similar data for a commercial sample of polyethylene, which is known to be highly branched,[2,3] are also plotted in Fig. 1. The melting temperature is lowered to 115° for the branched polymer and the melting range considerably extended in comparison with the linear one. The lowering of T_m and broadening of the melting range by branch units is in agreement with the predictions of the statistical equilibrium theory of crystallization in polymers.[4,5]

The melting temperature observed for polymethylene, 136 to 137°, is very close to the convergence temperature of 135° predicted for a high molecular weight *n*-paraffin by King and Garner[6] from an analysis of thermodynamic data for low molecular weight paraffins. This again illustrates the asymptotic relation between T_m and molecular weight in linear polymers.[4,5]

Recently a melting temperature of 132° has been reported[7] for a polymethylene prepared in a similar but not identical manner. This lower T_m may probably be attributed to the rapid heating rate (0.5°/min.) used in its determination. It has been

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[1] The work reported here was supported by the Office of Naval Research and the Office of the Quartermaster General.

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