The relationship of the pair, 4-nitro-2-propionylpyrrole [maxima at 247 mμ (log ε = 4.16); 300 mμ (log ε = 3.89); minimum at 278 mμ (log ε = 3.77)] and 4-nitro-2-acetylpyrrole [maxima at 245 mμ (log ε = 4.15) and 299 mμ (log ε = 3.81); minimum at 278 mμ (log ε= 3.80)], is established by the practical superposition of their ultraviolet spectra as is also that of 5-nitro-2-propionylpyrrole [maxima at 240 mμ (log ε = 4.03), 3.28 mμ (log ε = 4.15); minimum at 265 mμ (log ε = 3.38)] and 5-nitro-2-acetylpyrrole [maxima at 239 mμ (log ε = 4.00); 328 mμ (log ε = 4.11) and minimum at 264 mμ (log ε = 3.34)].

The structure of 1-methyl-4-nitro-2-pyrrolecarboxylic acid, m.p. 199–200° has been related to that of 4-nitro-2-acetylpyrrole by Anderson.[4] The synthesis of the ester of this acid by an unequivocal method has been reported.[5] This, on saponification, gave 1-methyl-4-nitro-2-pyrrolecarboxylic acid,[4] m.p. 199–200°. Decarboxylation of this acid gave 1-methyl-3-nitropyrrole,[4] m.p. 63–64°. This represents an absolute proof of the structures of all the nitro-2-acylpyrroles described.

EXPERIMENTAL[6]

4-Nitro-2-propionylpyrrole. The mixed 4-nitro and 5-nitro-2-propionylpyrroles (5.15 g.) previously reported as 5-nitro-2-propionylpyrrole[1] were dissolved in 300 ml. of 10% sodium carbonate solution and extracted ten times with 100 ml. portions of ether. The combined ether extracts were concentrated to a solid and crystallized from boiling water to yield very pale yellow crystals; yield, 2.02 g., m.p. 136–137°.

Anal. Calcd. for $C_7H_8N_2O_3$: C, 50.0; H, 4.8. Found: C, 50.3; H, 4.9.

5-Nitro-2-propionylpyrrole. The sodium carbonate solution after the extraction of the 4-nitro-2-propionylpyrrole was acidified using 10% sulfuric acid solution. The acidified solution was then extracted ten times with ether as previously described and the combined ether extracts concentrated to a solid. The solid residue was crystallized from boiling water to give yellow fibrous needles; yield, 0.975 g., m.p. 134–135°.

Anal. Calcd. for $C_7H_8N_2O_3$: C, 50.0; H, 4.8. Found: C, 50.5; H, 5.1.

A mixed melting point of the separated 4-nitro- and 5-nitro-2-propionylpyrroles was 102–104°. The melting point of the previously reported[1] unseparated isomers was 100–101°.

4-Nitro-2-propionylpyrrole semicarbazone. 4-Nitro-2-propionylpyrrole (3.0 g.), 4.0 g. of sodium acetate, and 4 g. of semicarbazide hydrochloride were dissolved in 100 ml. of warm water. After standing for 20 days, fine yellow needles had separated which were recrystallized from hot water; yield, 2.4 g., m.p. 229–230°.

Anal. Calcd. for $C_8H_{11}N_5O_3$: C, 42.7; H, 4.9. Found: C, 42.8; H, 4.6.

5-Nitro-2-propionylpyrrole semicarbazone. 5-Nitro-2-propionylpyrrole (0.98 g.) was treated with 1.0 g. of sodium acetate and 1.5 g. of semicarbazide hydrochloride in 100 ml. of 25% ethanol water solution. After standing for 20 days the yellow-orange product separated and was recrystallized from hot water; yield, 0.9 g., m.p. 211–212°.

Anal. Calcd. for $C_8H_{11}N_5O_3$: C, 42.7; H, 4.9. Found: C, 42.4; H, 4.7.

A mixed melting point of the 4-nitro- and 5-nitro-2-propionylpyrrole semicarbazones was 203–205°. The previously reported[1] semicarbazone of the unseparated isomers was 203–204°.

Acknowledgment. We are indebted to Dr. Al Steyermark and his associates for the microanalyses and Messrs. A. Motchane and S. Traiman for the ultraviolet spectra.

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(5) M. J. Weiss, J. S. Webb, and J. M. Smith, *J. Am. Chem. Soc.*, **79**, 1266 (1957).

(6) All melting points are corrected.

Chemistry of Hydrouracils. 1,3-Dihalohydrouracils

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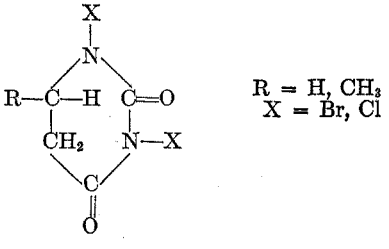
During the course of investigating the chemical and biological activity of various *N*-halogen compounds, the preparation of a number of heretofore unknown 1,3-dihalohydrouracils became of interest to us.



It was found that the efficiency of the halogenation in an aqueous medium was dependent on the *p*H at which the halogenation was carried out. Chlorination gave fair results (30–40% yield) when the reactions were carried out at a *p*H greater than 7 and gave good results (70–80% yield) when the reaction bath was maintained in the range *p*H 1–3. Bromination, on the other hand, was carried out successfully only at a *p*H greater than 4.

1,3-Dichlorohydrouracil, in concentrations as low as 1 p.p.m., completely inhibited the growth of the test organisms *Erwinia amylovora*, *Xanthomonas phaseoli*, *Micrococcus pyogenes* var. *aureus*, and *Escherichia coli*.[2] 4-Methyl-1,3-dichlorohy-

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(2) Biological data by Boyce Thompson Institute for Plant Research, Inc., Yonkers, N. Y.

drouracil gave 95–100% growth inhibition of these same organisms at a concentration of 1000 p.p.m. or greater.

The chlorine derivatives appear to be quite stable while the bromine compounds are somewhat less so. One sample of 4-methyl-1,3-dibromohydrouracil decomposed spontaneously after a few days while a companion sample remained undecomposed after some months. It would seem advisable that compounds of this type should be handled with some care.

EXPERIMENTAL[3]

1,3-Dichlorohydrouracil. Hydrouracil[4] (57 g., 0.5 mole) was suspended in one liter of water in a two-liter beaker furnished with a gas dispersion tube, a mechanical stirrer, and an addition funnel. The electrodes of a Beckman model H-2 *p*H meter were so arranged that the *p*H of the contents of the beaker could be followed continuously. Chlorine (75 g., 1.05 mole) was passed in over a 2-hr. period while 6*N* sodium hydroxide was added at such a rate as to maintain the *p*H of the reaction mixture in the range *p*H 1–3. The resulting solid was filtered off, washed with water, and dried. Yield 73 g. (80%). The solid crystallized from a mixture of chloroform and carbon tetrachloride to give white plates, m.p. 128–129°.

Anal. Calcd. for $C_4H_4Cl_2N_2O_2$: C, 26.2; H, 2.2; Cl, 38.8; N, 15.3; avail. Cl, 77.5. Found: C, 26.7; H, 2.4; Cl, 38.6; N, 15.2; avail. Cl., 76.5.

4-Methyl-1,3-dichlorohydrouracil. 4-Methylhydrouracil[5] (64 g., 0.5 mole) was chlorinated in the manner described above. A lower *p*H (1–2) seemed advantageous. The solid, after washing and drying, weighed 77 g. (78%). Crystallization from carbon tetrachloride gave white plates, m.p. 87–87.5°.

Anal. Calcd. for $C_5H_6Cl_2N_2O_2$: C, 30.4; H, 3.1; Cl, 36.0; N, 14.2; avail. Cl, 72. Found: C, 30.7; H, 3.0; Cl, 37.4; N, 14.2; avail. Cl, 71.7.

4-Methyl-1,3-dibromohydrouracil. 4-Methylhydrouracil (12.8 g., 0.1 mole) was suspended in 500 ml. of water in a one-liter beaker furnished as described above except that the gas dispersion tube was replaced with a second addition funnel. Bromine (37 g., 0.23 mole) was added dropwise over a one-hour period while the *p*H of the mixture was maintained in the range *p*H 6.5–8.6 by the addition of 6*N* sodium hydroxide. The pale yellow solid which remained after filtration, washing and drying, weighed 17.5 g. (61%) and melted at 130–131°.

Anal. Calcd. for $C_5H_6Br_2N_2O_2$: C, 21.2; H, 2.1; N, 9.8; avail. Br, 112. Found: C, 21.3; H, 2.0; N, 9.9; avail. Br, 111.

1,3-Dibromohydrouracil. Hydrouracil (11.4 g., 0.1 mole) was treated as above over a 1.8-hr. period. The pale yellow solid obtained after workup weighed 8 g. (30%) and melted 268–270° with decomposition.

Anal. Calcd. for $C_4H_4Br_2N_2O_2$: avail. Br, 118. Found: avail. Br, 117.9.

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(3) All melting points are uncorrected. Elemental analyses by Diamond Alkali Company Research Analytical Laboratory. Available halogen determinations by sodium thiosulfate titration. The percent available halogen is taken as twice the weight percent of halogen attached to nitrogen.

(4) J. S. Mackay and S. Frank, U. S. Patent 2,688,020 (1954).

(5) E. Fischer and G. Roeder, *Ber.* **34B**, 3751 (1901).

Synthesis of 3,8-Endomethylene-3-azabicyclo[3.2.1]octane (Cyclocamphidine)[1]

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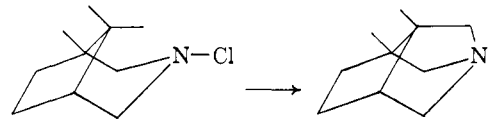
The free-radical chain decomposition of *N*-chloro secondary amines ("Hofmann-Loeffler-Freytag reaction")[2,3] has been used recently to effect the selective introduction of functional groups at the C_{18} (C/D fusion) angular methyl group in steroids.[4,5] We have also applied this useful technique in the camphor series to functionalize one of the "unactivated" π-methyl groups. Irradiation of *N*-chlorocamphidine (I) in sulfuric acid solution gave, after basification, a tertiary amine which was isolated as the crystalline hydrobromide in 67% yield. Chemical and physical evidence clearly show that the cyclocamphidine should be formulated as II. The infrared spectrum of the hydro-



I II

bromide lacks the absorption peak shown by camphidine hydrobromide at 1400 cm.$^{-1}$ which is characteristic of the *gem*-dimethyl grouping. The nuclear magnetic resonance spectrum of the cyclocamphidine hydrobromide (see Experimental) demonstrates the presence of only two methyl groups and is in complete accord with II.

The above synthesis of II, which doubtless can be effected conveniently on large scale from camphor, makes this one of the most readily available bridgehead amines.

EXPERIMENTAL

Camphidine hydrobromide. Camphidine, which has been prepared by the electrolytic reduction of camphoric imide,[6] was made by lithium aluminum hydride-reduction. Camphoric imide (6.2 g., 0.0343 mole) was dissolved in 150 ml. of tetrahydrofuran and added dropwise to a stirred slurry of 2.6 g. of lithium aluminum hydride in 75 ml. of tetrahydrofuran. The resulting mixture was refluxed with stirring for 11 hr., and then treated with water. The precipitate was

(1) This investigation was supported by fellowship AF-7544 to W. R. Hertler from the National Institute of Arthritis and Metabolic Diseases, Public Health Service.

(2) (a) A. W. Hofmann, *Ber.*, **18**, 5, 109 (1885); (b) K. Loeffler and C. Freytag, *Ber.*, **42**, 3427 (1909); (c) K. Loeffler, *Ber.*, **43**, 2035 (1910).

(3) For a brief review see R. Lukes and M. Ferles, *Coll. Czech.*, **20**, 1227 (1955).

(4) E. J. Corey and W. R. Hertler, *J. Am. Chem. Soc.*, **80**, 2903 (1958).

(5) P. Buchschacher, J. Kalvoda, D. Arigoni and O. Jeger, *J. Am. Chem. Soc.*, **80**, 2905 (1958).

(6) J. Tafel and K. Eckstein, *Ber.*, **34**, 3274 (1901).