The formula $\{H_3N\text{-}H\text{-}OH\}^0$ has been written to suggest that an un-ionized molecular entity similar to an ion pair exists in solution; this entity arises from the presumed hydrogen bonding between the nitrogen and oxygen atoms from the ammonia and water molecules. While this series of equilibria is reminiscent of a similar set for carbon dioxide and water, reference 4, there is no evidence and little reason to believe that with ammonia any of these steps is slow. Indeed, reaction 1 is undoubtedly a fast one to which only a Langevin time lag could be attributed; the same is true of reaction 2. Nevertheless, and presumably this may be attributed to the enhanced stability conferred by the hydrogen bond, there is a finite concentration of dissolved but unhydrated ammonia in the solution together with an amount of undissociated ammonium hydroxide, and, finally, an equilibrium concentration of ions, as is represented by equations 1 and 2. These facts were clearly established by Moore and Winmill,[7] from whose work on ammonia and alkyl substituted amine solutions the hydrogen bond concept arose.

The ratio of the concentrations of ammonia and undissociated ammonium hydroxide, equation 1, is independent of concentration if the concentrations be small, and may be termed B.

$$B = [NH_3]/[NH_4OH] \quad (3)$$

The value of B may be determined by measuring at at least three temperatures the ionization and the partition of ammonia between water and an immiscible solvent such as toluene. Moore and Winmill[7] thus determined how much of the undissociated ammonia in solution was present as dissolved ammonia and how much as ammonium hydroxide. Sidgwick[8] states that at 25° the value of B is 0.885. Using the relations

$$K(0)(\text{true}) = [NH_4^+][OH^-]/[NH_4OH] \quad (4)$$

$$K(0)(\text{apparent}) = \frac{[NH_4^+][OH^-]}{[NH_4OH] + [NH_3]} = \frac{[NH_4^+][OH^-]}{[NH_4OH](1 + B)} \quad (5)$$

$$= K(0)(\text{true})/(1 + B) \quad (6)$$

and the value of $K(0)$ (apparent) at 25° from reference 6, we find that the method of Moore and Winmill gives $K(0)$ (true) $= 3.34 \times 10^{-5}$, while Moore and Winmill themselves report $K(0)$ (true) at 20° from their measurements to be $5.2 \pm 1.3 \times 10^{-5}$. Bates and Pinching[6] give the values of $K(0)$ (apparent) at 20° and at 25° as 1.710 and 1.774×10^{-5}. The difference between the computed quantity 3.34×10^{-5} and Moore and Winmill's value of $5.2 \pm 1.3 \times 10^{-5}$ is thus too large to be accounted for by the limits of error specified, and is in the wrong direction as a function of temperature, unless other unaccounted potent factors affecting the true ionization constant in a different manner than the apparent constant were present.

We may employ the method described in reference 4 to obtain $K(0)$ (true) from the high field conductance data. From a series of plots of the coefficients A_2 and A_3 against b (see eq. 21, ref. 4), the reduced slope Q and the function ρ_0 (eq. 17, ref. 4) are obtained. From the data presented in Fig. 1 ρ_0 has the average value 0.1639, and, with the value for $K(0)$ (apparent) $= 1.77 \times 10^{-5}$, $K(0)$ (true) is found to be $6.3 \pm 0.5 \times 10^{-5}$. The precision of measurement is at least ten times poorer than for carbon dioxide, as may be seen from the discussion of errors in ref. 4. This value for $K(0)$ (true) must be compared with those in the paragraph above; it is larger than any of the values of $K(0)$ (true) either quoted or computed from other data. A larger $K(0)$ bespeaks a smaller Wien effect. It is indeed possible that electrolytic impurities might cause the measurements here reported to be low, although every precaution has been taken to exclude contaminants. It seems more probable that the rapidity of reactions 1 and 2 would give a high field conductance increase larger than would truly represent the equilibrium concentrations of the several ionic species at low fields and thus a $K(0)$ (true) which is too small. This possibility hinges upon the relative speeds of reactions 1 and 2, direct information on which is not available. Experiments at a variety of pulse lengths might help elucidate this point. It is planned to extend these measurements to a range of temperatures for which values of $K(0)$ (apparent) are available in order to test the internal consistency of data derived from the high field conductance measurements.

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(7) T. Moore and T. Winmill, *J. Chem. Soc.*, **101**, 1635 (1912); also, **91**, 1373 (1907).

(8) N. V. Sidgwick, "The Chemical Elements and their Compounds," Oxford University Press, New York, N. Y., 1950, p. 660.

Thiohydantoins of Amino Acids[1]

BY E. CAMPAIGNE AND WESLEY L. ARCHER[2]

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Recent reports[3] have shown that some thiosemicarbazones have an inhibitory effect on the growth of vaccinia viruses. Thompson and Wilkin have shown that the phenylalanine antagonist, β-2-thienylalanine, prevented the multiplication of vaccinia virus in chick embryonic tissues.[4] 5-Substituted thiohydantoins possess certain structural similarities to both of these types of virus inhibitors, having an α-aminocarbonyl and an N-substituted thiourea portion in the same molecule. In pursuing a program of virus chemotherapy[5] we have synthesized a number of thiohydantoins in order to determine whether these compounds had antiviral activity. Tests conducted by Dr. R. L. Thompson at the Indiana University Medical

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(2) Abstracted from the thesis of Wesley L. Archer, to be submitted to Indiana University in partial fulfillment for the Degree of Doctor of Philosophy.

(3) *Cf.* R. L. Thompson, S. A. Minton, Jr., J. E. Officer and G. A. Hitchings, *J. Immunology*, **70**, 229 (1953); D. Hamre, J. Bernstein and R. Donovick, *Proc. Soc. Exp. Biol. Med.*, **73**, 275 (1950).

(4) R. L. Thompson and M. L. Wilkin, *ibid.*, **68**, 434 (1948).

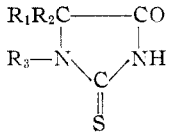
(5) *Cf.* E. Campaigne, *et al.*, THIS JOURNAL, **75**, 988 (1953).

School showed 5-phenyl-2-thiohydantoin, 5-(*p*-hydroxybenzyl)-2-thiohydantoin and the compounds described here to have no activity against several vaccinia strains.

We are reporting the synthesis of nine new thiohydantoins which are listed in Table I. The amino acids used were commercially available or easily prepared by standard methods with the exception of the 5-(2- and 3-thenyl)-thiohydantoins where the acetylated amino acids were employed. Deacetylation was acccomplished by refluxing the 1-acetyl-5-substituted thiohydantoin for one to two hours in sufficient 10% hydrochloric acid to obtain solution of the thiohydantoin. Deacetylation of 1-acetyl-5-(β-ethylmercaptoethyl)-2-thiohydantoin was accomplished without isolation of the solid acetyl intermediate.

TABLE I

5-SUBSTITUTED THIOHYDANTOINS



R_1	R_3	M.p., °C.[a]	Yield, %[b]	Nitrogen,[c] % Calcd.	Found
C_6H_5–[d]	CH_3CO	173.5–174[e]	36	11.28	11.50
p-ClC_6H_4–	CH_3CO	167–168[e]	71	9.91	10.23
p-BrC_6H_4–	CH_3CO	188–188.5[e]	65	8.56	8.46
$C_2H_5SCH_2CH_2$–	CH_3CO	58–58.5[f]	69	11.38	11.21
$C_2H_5SCH_2CH_2$–	H	99.5–100.5[g]	69	13.71	13.44
3-C_4H_3S–[h]	CH_3CO	157–158[e]	75	11.02	11.00
3-C_4H_3S–	H	177–178[g]	82	13.20	13.28
2-C_4H_3S–	CH_3CO	167–168[e]	92	11.02	11.15
2-C_4H_3S	H	197–198(dec.)[g]	93	13.20	13.09

[a] All melting points uncorrected, Fisher–Johns block. [b] Based on crude yields, the melting point of which is within 4° of that reported. [c] All analyses by Miss J. W. Dickey. [d] R_2 is methyl in this compound, H in all others. [e] Recrystallized from ethanol–water. [f] Recrystallized by slow evaporation of ethanol solution. [g] Recrystallized from water. [h] Originally synthesized by R. L. Hardin in this Laboratory.

Undoubtedly higher yields of some of the thiohydantoins could be realized if crude oily products were not sometimes encountered in the isolation. It was observed that prolonged mechanical stirring of an oily or semi-solid product in a water solution at ice-bath temperatures gave a better crystalline product. The thiohydantoins were finally recrystallized by dissolving in excess alcohol at room temperature and slowly adding water until saturation was reached, or by concentration under an air jet. Heating or extreme cooling of the recrystallizing medium led to various amounts of oily products.

Experimental

2-Thenylacetamidomalonic Acid.—Saponification of 7.7 g. (0.025 mole) of diethyl 2-thenylacetamidomalonate[6] with 25 ml. of 10% sodium hydroxide gave 5.9 g. (93.5%) of 2-thenylacetamidomalonic acid, which melted with evolution of carbon dioxide at 128.5–129°.

Anal. Calcd. for $C_{10}H_{11}O_5NS$: C, 46.70; H, 4.31. Found: C, 47.10; H, 4.49.

N-Acetyl-β-2-thienylalanine.—Decarboxylation was carried out on 5.6 g. (0.0218 mole) of 2-thenylacetamidomalonic acid in 50 ml. of water to give 4.0 g. (86%) of N-acetyl-β-2-thienylalanine, m.p. 128–129°.[7] A mixture of a sample of this compound with 2-thenylacetamidomalonic acid gave a depressed melting range.

1-Acetyl-5-(2-thenyl)-2-thiohydantoin.—The following procedure is typical of the thiohydantoin preparations. A solution of 4.0 g. (0.0188 mole) of N-acetyl-β-2-thienylalanine and 1.9 g. (0.025 mole) of ammonium thiocyanate in 5 ml. of glacial acetic acid and 25 ml. of acetic anhydride was refluxed on a steam-bath for one hour. The cooled solution was then added to 200 ml. of water with mechanical stirring to give 4.4 g. (92%) of cream colored crystals, m.p. 164–166°. Recrystallization from aqueous ethanol raised the melting point to 167–168°.

5-(2-Thenyl)-2-thiohydantoin.—A solution of 0.5 g. (0.002 mole) of 1-acetyl-5-(2-thenyl)-2-thiohydantoin in 25 ml. of 10% hydrochloric acid was refluxed for one hour, and then chilled to give 0.39 g. (93.5%) of 5-(2-thenyl)-2-thiohydantoin, which melted at 197–198° with decomposition after recrystallization from water.

5-(3-Thenyl)-2-thiohydantoin.—1-Acetyl-5-(3-thenyl)-2-thiohydantoin was prepared in an identical manner from N-acetyl-β-3-thienylalanine,[8] and readily deacetylated as above to yield white needles, melting at 177–178°.

(6) K. Dittmer, W. Herz and J. S. Chambers, *J. Biol. Chem.*, **166**, 541 (1946).

(7) K. Dittmer, *et al.*, THIS JOURNAL, **71**, 1202 (1949), reports the m.p. to be 130°.

(8) R. G. Garst, E. Campaigne and H. G. Day, *J. Biol. Chem.*, **180**, 1016 (1949).

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The Fluoroplatinates. II. Fluoroplatinic Acid

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The first paper in this series dealt with the preparation and properties of certain rare earth fluoroplatinates.[2] Prior to this, the only compounds containing the fluoroplatinate ion were certain ones from the alkali group elements.[3–5]

This paper is to report the preparation and isolation of fluoroplatinic acid.

Experimental

Fluoroplatinic Acid.—Lanthanum fluoroplatinate was prepared as previously described.[2] About 60 ml. of a 0.04 *M* solution of this salt was passed through an ion-exchange column at a rate of 3–4 ml. per minute. The dimensions of the column were 3.5 × 90 cm. and it was packed with 40–60 mesh Dowex-50 resin. The resin was hydrogen charged prior to the introduction of the salt solution.

The column was eluted with water at a rate of 3–4 ml. per minute. The yellow color of the fluoroplatinate ion appeared shortly after a liter of water had passed through the column. The elution process required less than two liters for its completion. The solution was stored in a polyethylene bottle. Tests for the lanthanum ion on this solution were negative.

A portion of this solution was evaporated to dryness in a polyethylene beaker by vacuum desiccation over sodium hydroxide pellets. Yellow crystals of hydrated fluoroplatinic acid were obtained.

This acid is hygroscopic and very soluble in water. The addition of a potassium salt to a solution of this acid precipitated the yellow crystalline potassium fluoroplatinate. The characteristic color of the iodoplatinate ion appeared slowly when iodide ion was added to the acid. Hydrogen was liberated when zinc was added to the acid.

Absorption Spectrum.—The absorption spectrum of the fluoroplatinic acid was measured with a Model DU Beckman spectrophotometer using matched 1-cm. cells. The curve was identical to that previously reported for the fluoroplatinate ion, having maxima at 275 and 318 mμ (not at

(1) Abstracted from a portion of the thesis to be submitted by Roy S. Clarke, Jr., in partial fulfillment of the requirements for the degree of Master of Arts.

(2) T. P. Perros and C. R. Naeser, THIS JOURNAL, **75**, 2516 (1953).

(3) H. Schlesinger and M. Tapley, *ibid.*, **46**, 276 (1924).

(4) A. G. Sharpe, *J. Chem. Soc.*, 3444 (1950).

(5) A. G. Sharpe, *ibid.*, 197 (1953).