After a 10% aqueous alkaline solution of this compound was boiled for 1 hour a 90% recovery could be effected on acidification.

Hydrochloride of β-Chloroethylaminopropane (XI). 1. **From 1-β-nitraminoethyl-1-propyl-3-nitrourea (X).**—To a suspension of 1.0 g. (0.0043 mole) of **XI** in 10 ml. of acetic acid was added 1.1 ml. (0.015 mole) of acetyl chloride. After 15 minutes at 45° the gas collected over water at 23° was 240 ml. The solvent was removed *in vacuo*, 5 ml. of absolute ethanol added and the distillation repeated. The residue was dissolved in 4 ml. of water and three extractions with 3-ml. portions of ether were carried out and then discarded. Evaporation of the aqueous solution left 0.445 g. of a gummy solid. This yielded 0.25 g., m.p. 249°, of white platelets when it was crystallized from hot ethanol (1.4 ml. per g.). When this 37% yield was twice recrystallized from ethanol the melting point was raised to 261–262°.

Anal. Calcd. for $C_5H_{13}NCl_2$: C, 38.0; H, 8.23; N, 8.86. Found: C, 37.8; H, 8.35; N, 8.86.

2. **From β-Hydroxyethylaminopropane.**—A solution of 1.5 g. (0.0146 mole) of 1-hydroxyethylaminopropane[9] in 2 ml. of chloroform was agitated with a stream of dry nitrogen while 7.3 ml. (0.06 mole) of thionyl chloride in 3 ml. of chloroform was added over 10 minutes. The solvent was boiled under reflux for 2 minutes and then distilled off, finally *in vacuo*. The solution obtained by addition of 5 g. of ice to the residue was extracted thrice with ether and the extracts discarded. Evaporation of the aqueous layer left 2.3 g. of crude β-chloroethylpropylamine hydrochloride. The crude material was crystallized from 3.7 ml. of absolute ethanol to give 1.84 g., m.p. 250–255°. The melting point of the 80% yield was raised to 262.8° by two recrystallizations from the same solvent. A mixed melting point with the product obtained by the first procedure was not lowered.

(9) H. Matthes, *Ann.*, **315**, 110 (1901).

TORONTO 5, CANADA RECEIVED JULY 19, 1950

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TORONTO]

Reaction of Acetyl Chloride with 1-Nitro-2-nitramino-2-propoxyimidazolidine

BY ROSS H. HALL AND GEORGE F WRIGHT[1]

The action of acetyl chloride on 1-nitro-2-nitramino-2-propoxyimidazolidine eliminates the primary nitramino group to leave the monoacid, propyl β-chloroethyliminonitrocarbamate. In alkaline solution the substance decomposes to yield β-aminoethylnitramine, while in acid solution it forms the monoacidic 1-β-chloroethyl-3-nitrourea. When this nitrourea is treated with alkali it forms the monoacidic 2-nitraminoöxazoline. The latter compound may be in mobile equilibrium with its tautomer, 2-nitriminoöxazolidone-2.

Examination of the elimination of the nitramino group by acetyl chloride has now been extended[2,3] to the addition product of propanol-1 to 1-nitro-2-nitriminoimidazolidone-2.[4] The cyclic structure of this addition product[5] has now been confirmed as 1-nitro-2-nitramino-2-propoxyimidazolidine by the potentiometric titration of a freshly-prepared alkaline solution which shows (Curve 1, Fig. 1) that it is a monobasic acid with K_A approximately 1×10^{-6}. This curve is not altered when the alkaline solution is aged for one week prior to titration.

When 1-nitro-2-propoxy-2-nitraminoimidazolidine is treated with acetyl chloride in an excess of acetic acid previously saturated with hydrogen chloride one product is obtained. On the basis of its elemental analysis and the potentiometric titration of its freshly-prepared alkaline solution (Curve 2, Fig. 1, $K_A = 2 \times 10^{-4}$) which shows it to be monoacidic, this compound is thought to be 1-chloroethyl-3-nitrourea (III). Titration of an aged sample (curve identical with 2, Fig. 1) shows it to be quite stable toward dilute aqueous alkali at 25°. However, hot aqueous alkali or prolonged treatment with acetyl chloride converts it to β-chloroethylamine.

If the acetyl chloride is used with acetic acid which initially contains no hydrogen chloride then only a small amount of III is obtained, and another product is obtained instead. This is understandable since the alternative product may be converted to III by treatment with hydrochloric acid. This hydrolysis releases propanol-1. Since a freshly-prepared alkaline solution of this substance is found by potentiometric titration to be monoacidic (curve 3, Fig. 1, $K_A = 7 \times 10^{-11}$) it is thought to be the propyl ester of β-chloroethyliminonitrocarbamate, II. Titration of an alkaline solution of II aged 36 hours gives the anomalous

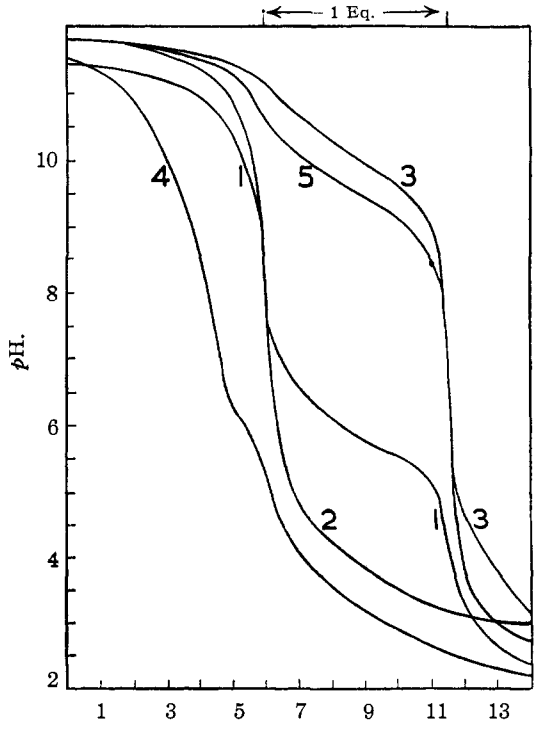


Fig. 1.

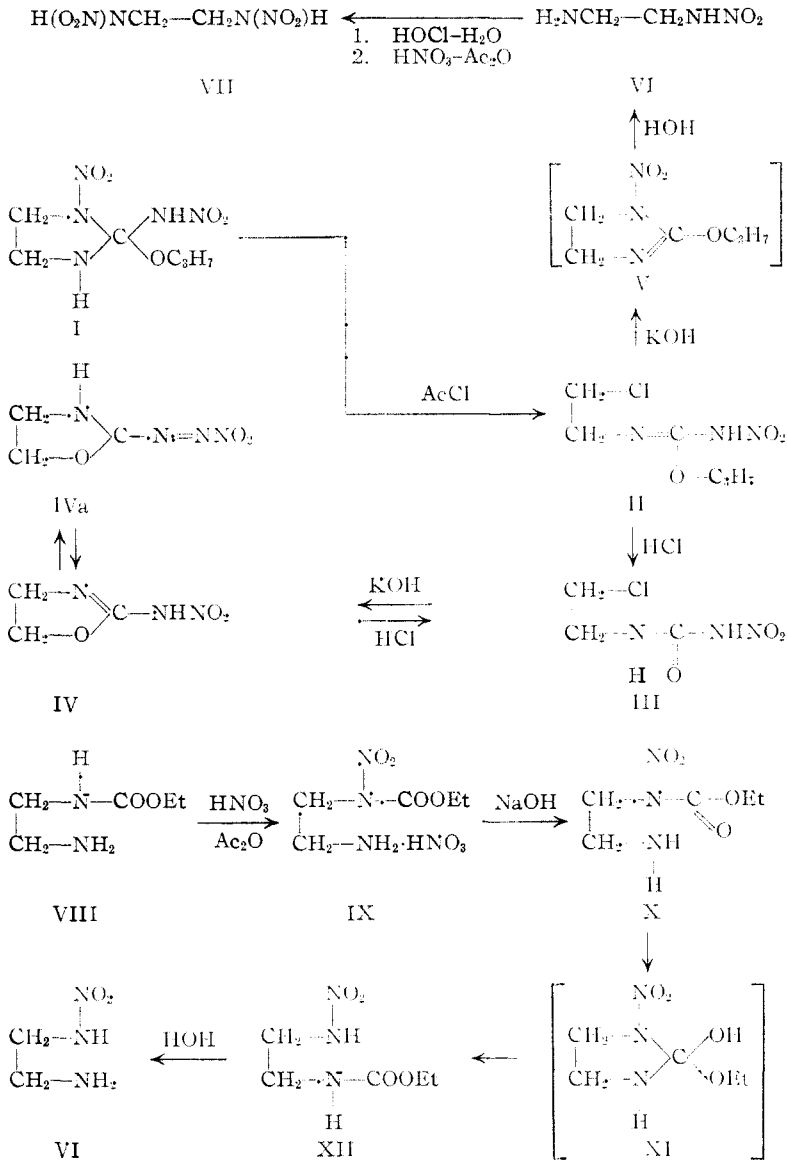
(1) Senior author.

(2) R. H. Hall, A. F. McKay and G. F Wright, THIS JOURNAL, **73**, 2205 (1951).

(3) R. H. Hall and G. F Wright, *ibid.*, **73**, 2208 (1951).

(4) S. S. Barton, R. H. Hall and G. F Wright, *ibid.*, **73**, 2201 (1951).

(5) A. F. McKay and G. F Wright, *ibid.*, **70**, 3990 (1948).



curve 4, Fig. 1. This seems to indicate that decomposition has occurred; indeed none of compound II can be recovered from the acidified solution.

When propyl β-chloroethyliminonitrocarbamate (II) is boiled with ethanolic potassium hydroxide and then acidified slightly with hydrochloric acid, an acid is precipitated. Potentiometric titration shows that it is a typical amino acid with K_A and K_B approximately 2 and 5 × 10^{-10}, respectively. According to its analysis it is β-aminoethylnitramine (VI) This structure has been confirmed by converting the substance to 1,2-dinitraminoethane (VII) *via* the dichloramine,[6] and by hydrolysis of ethyl β-nitraminoethylcarbamate, XII. The constitution of XII has been established by its elemental analysis and by its potentiometric titration as a monoacid of correct molecular weight and pK approximately 10^{-6}, like most saturated aliphatic primary nitramines. Its preparation is of interest because the reaction seems to involve the migration of a carboethoxyl group.

When ethyl β-aminoethylcarbamate, VIII,[7] was nitrated either with nitric acid or nitric acid–acetic anhydride mixture the expected nitrate salt, IX, of ethyl β-aminoethylnitrocarbamate, X, was obtained. When an aqueous solution of this amine salt was made alkaline and then acidified to *p*H 6.5, ethyl β-nitraminoethylcarbamate, XII, was precipitated instead of the salt of the primary amine, X. This would apparently involve the migration of the carboethoxyl group from the nitramino to the amino nitrogen but may be explained satisfactorily by assuming that the cyclic intermediate, XI, forms and then decomposes principally by one of its three possible modes of decyclization. The formation of such intermediates seems to be the rule among β-substituted ethylcarbamates.[2,3]

One may presume that β-aminoethylnitramine is the hydrolytic product from 1-nitro-2-propoxy-Δ^2-imidazoline (V) which would be formed initially by loss of hydrogen chloride from II in alkaline medium. Ring closure must thus be effected with retention of the propoxy group.

On the other hand, when 1-β-chloroethyl-3-nitrourea (III, which has lost the propoxy group) is treated with hot ethanolic potassium hydroxide, potassium chloride is precipitated, and acidification yields a substance which is thought to be 2-nitraminoöxazoline (IV). The alternative structure, 1-nitroimidazolidone-2, is considered to be improbable because the compound cannot be converted to dinitroimidazolidone with the nitrating agents commonly used with this type of substance. Furthermore the compound will revert to 1-chloroethyl-3-nitrourea (III) when it is warmed with dilute hydrochloric acid. This interconvertibility is characteristic of oxazolones.

The acidic function of IV can be demonstrated by potentiometric titration of a freshly-prepared alkaline solution. The titration (curve 5, Fig. 1) is characteristic of a very weak acid (K_A approximately 2.5 × 10^{-10}) resembling the aci-form of nitroguanidine.[4]

Although the titration would indicate that IV was a primary nitramine, it may be significant that this group cannot be eliminated by acetyl chloride which, instead, regenerates 1-chloroethyl-3-nitrourea. This inactivity toward acetyl chloride might be considered as evidence for the alternative structure, 2-nitriminoöxazolidone-2 (IVa). In this event a much more labile tautomerism must be

(6) G. N. R. Smart and G. F. Wright, *Can. J. Research*, **B26**, 281 (1948).

(7) T. S. Moore, M. Boyle and V. M. Thorn, *J. Chem. Soc.*, **39**, (1929).

postulated for the oxazoline–oxazolidone series than has been observed in the imidazoline–imidazolidone series. Supporting evidence that the compound is IVa is shown by the reddish Franchimont test which it gives with dimethylaniline. This Franchimont test is identical with that given by 2-nitriminoimidazolidone-2.

Experimental[8]

1-Nitro-2-propoxy-2-nitraminoimidazolidine (I).—The 1-nitro-2-propoxy-2-nitraminoimidazolidine used in these experiments was prepared according to the procedure of A. F. McKay and G. F Wright.[5] The crude yield reported by these authors was increased to 37% by slight modification of the procedure. Absolute *n*-propyl alcohol was used. Also, the alkali treatment of the residue was eliminated. Instead, after the solution had been concentrated by a factor of ten, it was seeded with a crystal of the pure material and chilled for several hours. The crude material, m.p. 109–113°, was boiled in ten times its weight of water for 5 minutes in order to destroy unchanged starting material. Two crystallizations of the recovered material (91%) from ethanol yielded white needles melting at 125.0–125.5° (26% over-all yield).

Propyl β-Chloroethyliminonitrocarbamate (II).—To a suspension of 11.7 g. (0.05 mole) of 1-nitro-2-propoxy-2-nitraminoimidazolidine (I) was added 11.8 ml. (0.0167 mole) of fractionally distilled acetyl chloride. The heterogeneous mixture was kept at a temperature of 50° for 3 hours, during which time 700 ml. of nitrous oxide (62.5% of theoretical for replacement of one nitramine group) was collected over water and identified by combustion analysis with hydrogen. After cessation of gas evolution, the clear liquid was evaporated *in vacuo* and two 25-ml. portions of absolute methanol were added with vacuum evaporation after each addition. Six ml. of chloroform was added to the residue and after several hours at 4° a precipitate weighing 3.4 g., m.p. 42–44°, could be obtained. Slow evaporation of the filtrate yielded another 2 g. melting at 41–44°. The crude yield of 5.4 g. is 51.7%. The crude product was contaminated with approximately 1% of 1-β-chloroethyl-3-nitrourea, which was easily removed by trituration with 0.1 *N* sodium hydroxide (7 ml. per g.), filtering, and washing the precipitate with three 2-ml. portions of water. Two such treatments raised the melting point to 50.5–51° and two crystallizations from absolute ether (3 ml. per g.) raised the melting point to 51.8–52.0°.

Anal. Calcd. for $C_6H_{12}N_8O_3Cl$: C, 34.4; H, 5.73; N, 20.1; Cl, 16.9. Found: C, 34.1; H, 5.70; N, 20.3; Cl, 16.9.

If this compound is boiled with an excess of 10% alcoholic silver nitrate for 1 hour, a precipitate of silver chloride does not appear. At the end of this time only 60% of the starting material is recovered, and if the solution is boiled for 5 hours only a 30% recovery is effected. There is a possibility that propyl chloride is being formed but there is no confirmation of this.

Although this compound seems not to react with silver nitrate, treatment with alcoholic potash yields a chlorine-free compound. A solution of 0.5 g. (0.0024 mole) of propyl β-chloroethyliminonitrocarbamate (II) and 0.4 g. (0.0075 mole) of potassium hydroxide in 4.4 ml. of 95% ethanol was refluxed for 5 minutes. The solution was neutralized, filtered and evaporated in an air stream. The residue (0.23 g.) was crystallized from 0.5 ml. of water to yield a product, m.p. 243°. A further crystallization from water raised the melting point to 244.8°. The compound is insoluble in ethanol. No halogen test is obtained with boiling silver nitrate. *Anal.* Calcd. for $C_2H_7N_3O_2$: C, 22.9; H, 6.66; N, 39.9. Found: C, 23.0; H, 6.71; N, 40.0. The compound evolves a colorless gas when its aqueous solution is treated with nitrous acid. Potentiometric titration shows that it is β-aminoethylnitramine (VI).

1,2-Dinitraminoethane (VII).—To 0.1 g. (95×10^{-6} mole) of the β-aminoethylnitramine was added a solution of 0.6 g. (72×10^{-4} mole) of sodium bicarbonate in 3.2 ml. of water. Chlorine was passed through this solution at 10° for 6 hours. The green oil was dissolved in 20 ml. of ether and then washed with cold 5% aqueous sulfuric acid and twice with water. After drying with magnesium sulfate the ether was evaporated. The residual oil was dissolved in 0.4 ml. (43×10^{-4} mole) of acetic anhydride and chilled to −80°. After 0.15 ml. (36×10^{-4}) mole of 99% nitric acid was added the whole was let warm to room temperature over 25 minutes, then chilled and poured into 2 ml. of 50% aqueous alkali containing 3 g. of ice. The mixture was acidified with 45% aqueous sulfuric acid and extracted four times with a total of 40 ml. of ether. After drying the extract with sodium sulfate the ether was evaporated to leave 0.01 g. of 1,2-dinitraminoethane. The melting point (178°) was not lowered by admixture with an authentic specimen. This 7% over-all yield of pure material should be compared with the 15% yield obtained by hypochlorination and nitration of ethylenediamine.[6]

1-β-Chloroethyl-3-nitrourea (III). 1. **From 1-Nitro-2-propoxy-2-nitraminoimidazoline** (I).—A saturated solution of hydrogen chloride in acetic acid was prepared by bubbling dry hydrogen chloride through anhydrous acetic acid. To 100 ml. of this solution 11.7 g. (0.05 mole) of 1-nitro-2-propoxy-2-nitraminoimidazoline (I) and 11.8 ml. (0.0167 mole) of acetyl chloride were added. The mixture was heated to 50° for 3 hours during which 750 ml. of nitrous oxide was collected over water. After cessation of gas evolution, the mixture was cooled and diluted with 20 ml. of water. The clear solution was evaporated *in vacuo* and the residual oil dissolved in 50 ml. of hot chloroform. Upon cooling, a precipitate of 1-β-chloroethyl-3-nitrourea (III) weighing 4.4 g., m.p. 113.5–114.2°, was obtained.

Concentration of the filtrate yielded a second crop of crystals melting at 112.5–114.5°. The combined yield of 5.56 g. is 67% of theory. Two crystallizations from chloroform (10 ml. per g.) raised the melting point to 116.3–117.2°. This precipitate gave a positive test with silver nitrate solution on heating.

Anal. Calcd. for $C_3H_6N_3O_3Cl$: C, 21.5; H, 3.58; N, 25.1; Cl, 21.1. Found: C, 21.7; H, 3.68; N, 25.2; Cl, 21.4.

2. **From Propyl β-Chloroethyliminonitrocarbamate** (II).—A solution of 1.0 g. of II in 9 ml. of concentrated hydrochloric acid was warmed on a steam-bath for 5 minutes, during which time the solid slowly dissolved. After one hour at 4°, filtration yielded 0.55 g. of a solid melting at 113–115°. Evaporation of the filtrate *in vacuo* to near-dryness precipitated a second crop of crystals weighing 0.19 g., m.p. 113–115°. The 0.74 g. of crude 1-β-chloroethyl-3-nitrourea then constitutes a 92.5% yield. One crystallization from ethanol (1 ml. per g.) yielded white needles melting at 115–115.5°. A mixed melting point with the product obtained when 1-nitro-2-propoxy-2-nitraminoimidazolidine (I) is treated with acetyl chloride, was not lowered.

β-Chloroethylamine Hydrochloride from 1-β-Chloroethyl-3-nitrourea (III). 1. **With Sodium Hydroxide.**—A solution of 0.5 g. of 1-β-chloroethyl-3-nitrourea (III) in 10 ml. of 5% aqueous sodium hydroxide was boiled under reflux for 5 minutes. The solution was cooled and extracted four times with a total of 40 cc. of ether. The ether was dried over sodium sulfate, then saturated with dry hydrogen chloride. Filtration yielded a precipitate weighing 0.069 g., m.p. 141–144° (yield 20%), which on crystallization from ethanol melted at 147–147.5°. Admixture of this compound with an authentic sample of β-chloroethylamine hydrochloride[6] did not lower the melting point.

2. **With Acetyl Chloride.**—To 10 ml. of acetic acid was added 1.0 g. (0.006 mole) of 1-β-chloroethyl-3-nitrourea and 2.0 ml. (0.028 mole) of acetyl chloride. The mixture was heated under reflux at 90° for 4 hours. The solvent was removed *in vacuo*, and 3 ml. of absolute ethanol added to the residue which was subsequently evaporated. Two ml. of ether was added to the residue and a gummy precipitate resulted. Crystallization from ethanol yielded 0.10 g., m.p. 146.5–148°, which constitutes a 14.5% yield. The melting point was not lowered when this compound was mixed with an authentic sample of β-chloroethylamino hydrochloride.

2-Nitraminoöxazoline (IV).—To 10 ml. of 95% ethanol was added 1.0 g. (0.006 mole) of 1-β-chloroethyl-3-nitrourea (III) and 0.9 g. (0.016 mole) of potassium hydroxide. The solution was refluxed on a steam-bath for 3 minutes, then chilled, neutralized with concentrated hydrochloric acid, and filtered. The precipitate was washed with three

(8) All melting points have been corrected against reliable standards.

1.0-ml. portions of absolute ethanol, after which the filtrate and washings were evaporated in an air stream. Crystallization of the residue from 0.8 ml. of nitromethane yielded 0.5 g., m.p. 111–112°. The yield is 80% of theory on the basis of III to IV. Three crystallizations from nitromethane raised the melting point to 113–113.2°.

Anal. Calcd. for $C_3H_5N_3O_3$: C, 27.45; H, 3.82; N, 32.1. Found: C, 27.30; H, 3.69; N, 31.7.

This compound is easily converted to the starting material (1-β-chloroethyl-3-nitrourea). A mixture of 0.5 g. (0.004 mole) of IV in 2.0 ml. of 18% hydrochloric acid was warmed on a steam-bath for 6 minutes during which time the solid dissolved. Upon chilling, 0.55 g., m.p. 113–116°, was obtained, which constitutes an 86% yield. Admixture of this compound with 1-β-chloroethyl-3-nitrourea did not lower the melting point.

Similarly, when IV is treated with boiling acetyl chloride, 1-β-chloroethyl-3-nitrourea is obtained. A solution of 0.20 g. (0.0015 mole) of IV in 5.0 ml. of acetyl chloride was refluxed under dry nitrogen for 3 hours. The solvent was distilled off and 0.75 ml. of absolute ethanol added to the residue. A precipitate of 0.1 g., m.p. 98–104° (39% of theory), was obtained. Crystallization from 0.5 ml. of ethanol raised the melting point to 111–113.5°. The melting point was not lowered when this sample was mixed with a sample of 1-β-chloroethyl-3-nitrourea.

2-Nitraminoöxazoline (IV) with Nitric Acid.—To 10 ml. of 100% nitric acid stirred by a stream of dry nitrogen, was added over a 6-minute period 1.0 g. (0.0076 mole) of IV. The temperature was maintained at 3° during the addition of the compound, after which the solution was warmed to 22° for 25 minutes. The solution was poured over 100 g. of ice, but no precipitate appeared. The clear aqueous solution was evaporated to dryness *in vacuo* leaving a trace of an oil which resisted attempts to crystallize. An identical procedure as described above resulted in an 88% yield of N,N'-dinitroethyleneurea from ethyleneurea.

2-Nitriminoöxazolidine (IV) with Diazomethane.—To a solution of 0.5 g. (0.0037 mole) of IV in 5.0 ml. of absolute ethanol was added 15 ml. of an ethereal solution of diazomethane. The mixture was stirred at 4° for 90 minutes during which time the solid slowly dissolved. The solvent was removed by distillation and the residue dissolved in 1.5 ml. of 5% sodium hydroxide. This solution was extracted five times with a total of 15 ml. of ether. The ether extract was dried over sodium sulfate and evaporated, leaving 0.1 g. of an oil which is water soluble but forms a cloudy solution in acid. The acidified aqueous layer was extracted four times with a total of 12 ml. of chloroform. Evaporation of this extract *in vacuo* left only a trace of an oil.

Potentiometric Titrations.—The potentiometric titrations were performed with a Coleman Electrometer. In each case 0.00063 mole of the compound was dissolved in an excess of 15 ml. of 0.0867 *N* NaOH and titrated with 0.1140 *N* HCl, except in the titration of β-aminoethylnitramine (VI). A solution of 55×10^{-5} mole of this compound was dissolved in 10.2 ml. of 0.1140 *N* alkali and titrated immediately with 0.1140 *N* HCl. Three inflections were observed in the titrimetric curve: with 5 ml. acid at *p*H 10.7; 10.2 ml. acid at *p*H 7.4; and 15.5 ml. acid at *p*H 3.0. The substance is thus a typical amino-acid with the expected formula weight.

Ethyl β-Aminoethylnitrocarbamate Nitrate (IX).—To a solution of 30 ml. (0.73 mole) of 99% nitric acid and 15 ml. (0.15 mole) of acetic anhydride in a Dry Ice-bath was added 5 ml. (0.043 mole) of ethyl β-aminoethylcarbamate over 1 hour. The reaction mixture was warmed to 0° over 1 hour and then poured on 300 g. of ice. The aqueous solution was evaporated to dryness *in vacuo* and the residue dissolved in 50 ml. of ethanol. Addition of 50 ml. of ether caused precipitation of 7.9 g., m.p. 79–80° (87% yield). Three crystallizations from ethanol (2.2 ml. per g.) raised the melting point to 82.5–83.5°. The product is very water soluble and it gives a precipitate with nitron. It does not decolorize Karl Fischer reagent.

Anal. Calcd. for $C_6H_{12}N_4O_7$: C, 25.0; H, 5.00; N, 23.3. Found: C, 25.1; H, 5.19; N, 23.4.

Ethyl β-Nitraminoethylcarbamate (XII).—A solution of 2.4 g. (0.01 mole) of IX in 5 ml. of water was made slightly alkaline with 2.5 *N* aqueous NaOH and then acidified with 6 *N* HCl. The water-washed precipitate weighed 1.75 g. (99% yield) and melted at 87–90°. Three crystallizations from ethanol (2 ml. per g.) raised this melting point to 88.5–90.5°. The molecular weight was determined by potentiometric titration of the sodium salt with hydrochloric acid: calcd. 177; found 175.

Anal. Calcd. for $C_5H_{11}N_3O_4$: C, 33.9; H, 6.21; N, 23.7. Found: C, 33.9; H, 6.35; N, 23.9.

β-Aminoethylnitramine (VI).—A solution of 0.37 g. (0.0021 mole) of XII in 2.5 ml. of 2.5 *N* aqueous sodium hydroxide was boiled for 1 hour under reflux. Neutralization with concd. hydrochloric acid precipitated 40% of unchanged XII. The filtrate was evaporated to dryness at 20–30° and the residue crystallized from 1 ml. of water. The yield of β-aminoethylnitramine (m.p. 240°) was 0.021 g. or 12% of theoretical. A mixed melting point with the substance obtained from propyl β-chloroethyliminonitrocarbamate (II) was not depressed.

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[CONTRIBUTION FROM THE WARNER INSTITUTE FOR THERAPEUTIC RESEARCH]

α-Thienyl Substituted Aminoesters with Analgetic and Spasmolytic Properties

BY FREDERICK LEONARD AND IRVING EHRENTHAL[1]

A series of ethyl 4-dialkylamino-2-phenyl-2-α-thienyl)- and 2,2-di-(α-thienyl) alkanoates was synthesized for pharmacological study and for conversion to "α-thienyl-methadone" and its homologs. The aminoacid esters were prepared by alkylating the appropriately disubstituted ethyl acetate with basic-alkyl chlorides. Compounds of the methadone series could not be obtained by the action of Grignard reagents on either the intermediate disubstituted acetates or the 4-dialkylaminoalkanoates. None of the esters demonstrated appreciable antispasmodic or analgetic activity and are apparently less effective than their benzene isosteres.

Esters of aminodiarylalkanoic acids (I) which are useful as antispasmodics and analgetics have been described[2] in the patent literature. In view of the lack of quantitative data on esters of this type, their marked structural similarity to, and the theoretical possibility of their conversion to congeners of 6-dimethylamino-4,4-diphenyl-3-heptanone (methadone, II), a number of ethyl 4-dialkylamino-2-phenyl-2-(α-thienyl)- and 2,2-di-(α-thienyl)-alkanoates (VI) were prepared for pharmacological evaluation and use in the synthesis of "thienyl-methadone" and its homologs.

$ROOCC(Ar)_2C_nH_{2n}Am$

I

$H_5C_2COC(C_6H_5)_2CH_2CH(CH_3)N(CH_3)_2$

II

The Grignard reaction between ethyl α-thienylglyoxylate (III) and α-thienylmagnesium bromide or phenylmagnesium bromide gave the glycolic

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(2) M. Bockmühl and G. Erhart, U. S. Patent 2,250,771 [*C. A.*, **35**, 3391 (1941)].