problem is particularly serious for homarine, which is very temperature sensitive and decarboxylates readily, with the formation of dark solutions.

The best solution to the problem is to use a strong base ion-exchange resin to hydrolyse an ester rather than to neutralize the acid salts. The heating problem mentioned above is eliminated, as the saponification of the ester salt is not particularly exothermic. The procedure has the added advantage in that the ester methiodides can be easily purified by recrystallization before use, in contrast to the methiodides of the free acids which are difficult to separate from unreacted acid.

The eluate from passage of the ester methiodide through a strong base hydroxide column is neutral, colorless, and iodide free. Evaporation of the aqueous solutions using a rotary evaporator at room temperature readily affords the hydrated betaines in colorless crystalline form of high purity and in high yield.

EXPERIMENTAL[6]

1-Methyl betaine of isonicotinic acid. A solution of 5.00 g. (17.0 mmoles) of 1-methyl-4-carbomethoxy pyridinium iodide, m.p. 189–191° dec.,[7] in 50 ml. of water was passed through a 2 cm. × 15 cm. column of Dowex-1 in the hydroxide form. The column was eluted with 50 ml. of water and the neutral, colorless, iodide free eluate evaporated on a rotary evaporator at room temperature to a semisolid paste. To this was added 10 ml. of ethanol and the white solid filtered, giving 2.08 g., m.p. 286–289° (immediate decrepitation and loss of water when the sample was placed in the melting point apparatus, decomposition at the melting point). The addition of a few milliliters of ether to the mother liquor afforded an additional 0.28 g., m.p. 286–288°. Total yield 89.5%. Reported[8] m.p. 264° (anhydrous).

Anal. Calcd. for $C_7H_7O_2N \cdot H_2O$: C, 54.19; H, 5.85; N, 9.03. Found: C, 54.31; H, 5.63; N, 8.97.

Picrate of 1-methyl betaine of isonicotinic acid. To a solution of the betaine in alcohol was added a saturated alcoholic solution of picric acid, giving a yellow picrate, m.p. 214–216°; reported[4] m.p. 215–217°.

Anal. Calcd. for $C_{13}H_{10}O_9N_4$: C, 42.63; H, 2.75; N, 15.30. Found: C, 42.87; H, 2.74; N, 15.49.

Trigonelline. A solution of 5.00 g. (17.0 mmoles) of 1-methyl-3-carbomethoxy pyridinium iodide, m.p. 128–130° dec.[8] in 50 ml. of water was passed through a 2 cm. × 15 cm. column of Dowex-1 in the hydroxide form. The column was eluted with 50 ml. of water and the neutral, colorless, iodide free eluate evaporated on a rotary evaporator at room temperature to a semisolid paste. To the paste was added 10 ml. of ethanol and the white crystalline solid filtered off, giving 1.70 g., m.p. 230–233° (immediate decrepitation and loss of water when the sample was placed in the melting point apparatus, decomposition at the melting point). The addition of a few milliliters of ether to the mother liquor gave an additional 0.60 g., m.p. 230–233°. Total yield 87.4%. Reported[9] m.p. 218°.

Anal. Calcd. for $C_7H_7O_2NH_2O$: C, 54.19; H, 5.85; N, 9.03. Found: C, 53.80; H, 6.02; N, 9.01. Several analyses of the trigonelline hydrate were made by several microanalytical laboratories. The first two analyses were high in carbon by about 0.40%. The third sample was recrystallized from alcohol and was low in carbon by 0.39%, and is the one reported here.

Trigonelline picrate. To an alcoholic solution of trigonelline was added a saturated solution of picric acid in alcohol, giving a yellow picrate, m.p. 204–205°, reported[9] 205–206°.

Anal. Calcd. for $C_{13}H_{10}O_9N_4$: C, 42.63; H, 2.75; N, 15.30. Found: C, 42.76; H, 2.74; N, 15.52.

Homarine. A solution of 5.00 g. (17.0 mmoles) of 1-methyl-2-carbethoxy pyridinium iodide, m.p. 108–109,[8] in 50 ml. of water was passed through a 2 cm. × 18 cm. column of Dowex-1 in the hydroxide form and eluted with 50 ml. of water. The neutral, colorless, iodide free eluate was evaporated on a rotary evaporator at room temperature to a semisolid paste. To the paste was added 10 ml. of ethanol and the betaine filtered off to give 0.80 g. To half of the mother liquor was added a small amount of ether giving an additional 0.55 g., making the yield 58%. The material does not have a melting point, but slowly carbonizes when heated. Solutions of this betaine must not be heated or decomposition takes place.

Anal. Calcd. for $C_7H_7O_2N$: C, 61.31; H, 5.15; N, 10.21. Found: C, 61.31; H, 4.95; N, 9.98.

Homarine picrate. To the other half of the mother liquor mentioned above was added a saturated alcoholic picric acid solution to give an orange picrate, m.p. 158–160°, reported[4] 155–160°.

Anal. Calcd. for $C_{13}H_{10}O_9N_4$: C, 42.63; H, 2.75; N, 15.30; Found: C, 42.47; H, 2.84; N, 14.76.

Acknowledgment. Analyses were made by Scandinavian Microanalytical Labs., Box 1257, Copenhagen 5, Denmark; Spang Microanalytical Labs., P.O. Box 1111, Ann Arbor, Mich.; and Hufmann Microanalytical Laboratories, 3830 High Court, P.O. Box 125, Wheatridge, Colo.

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[6] All melting points are uncorrected. All melting points were taken by placing the samples in the melting point apparatus approximately 10° before the melting point to minimize premature decomposition.

[7] E. M. Kosower, *J. Am. Chem. Soc.*, **80**, 3253 (1958).

[8] E. M. Kosower, J. A. Skorcz, W. M. Schwarz, Jr., and J. W. Patton, *J. Am. Chem. Soc.*, **82**, 2188 (1960).

[9] E. Schulze, *Z. physiol. Chem.*, **60**, 155 (1909).

Preparation of Polyvinylamine Perchlorate[1]

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The synthesis of poly(vinylamine) and its derivatives has been detailed by Reynolds and Kenyon.[3] Since various other derivatives of poly(vinylamine) (V) were of interest as potential constituents of propellants, the synthesis of the polymer was under-

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[2] The authors are indebted to Dr. E. C. Horswill, Mr. P. McWain, and Mr. A. Reife for assistance in the early stages of this investigation.

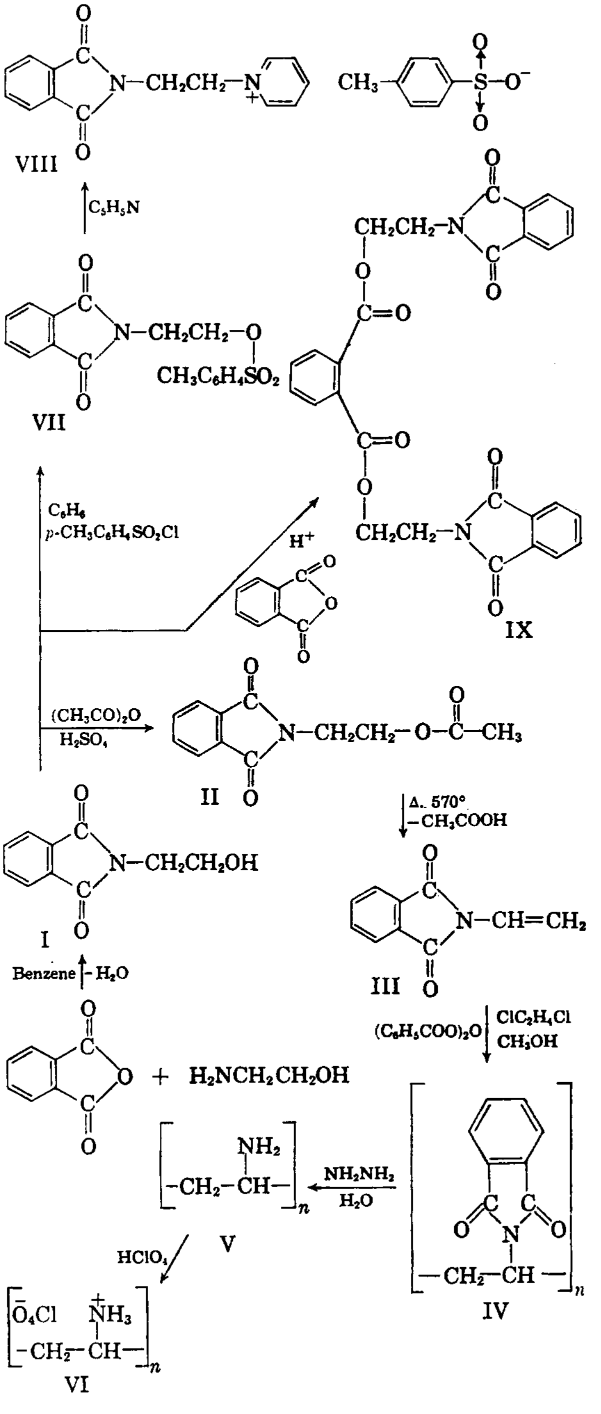
[3] D. D. Reynolds and W. O. Kenyon, *J. Am. Chem. Soc.*, **69**, 911 (1947).

taken following the general method of Reynolds and Kenyon.

In our hands, the preparation of 2-phthalimidoethyl acetate (II) described by Hanford and Stevenson[4] was improved and simplified by elimination of the laborious distillations of the intermediate, 2-phthalimidoethanol (I), and the final product. The intermediate was not isolated but was directly acetylated and the 2-phthalimidoethyl acetate was isolated by crystallization in 90% yield after removal of the acetylation by-products by distillation.

The 2-phthalimidoethyl acetate was pyrolyzed[4] and the resulting *N*-vinylphthalimide (III) was polymerized[3] following known techniques in an over-all yield of about 70% for the two steps. Hydrazinolysis of the poly(*N*-vinylphthalimide) (IV) was effected following the method of Reynolds and Kenyon[3] but their method for preparation of the hydrogen halide salts was modified for the synthesis of the perchloric acid salt of poly(vinylamine) (VI). Thus, the hydrazinolysis mixture was diluted with water and steam-distilled to remove the excess hydrazine. The resulting solution was acidified with perchloric acid and the insoluble phthalhydrazide was filtered. After dialysis of the filtrate, the solution was treated with Amberlite IRA-400 (OH^-) resin and reacidified with perchloric acid. Lyophilization of the resulting solution (*p*H 3.0) after freezing afforded a product that contained less perchloric acid than required by stoichiometry. The deficiency was eliminated by dissolving the solid in water and treating with the calculated amount of the acid. Lyophilization then gave poly(vinylamine perchlorate) (VI) with the correct analytical composition. The light-brown, hygroscopic, polymeric perchlorate salt had physical properties similar to the halide salts[3] except that it could be detonated by strong heating or by a firm hammer blow on a steel anvil. The molecular weight, 90,000 (D. P. 630), was determined using a light-scattering technique.

During the course of this investigation, two new compounds, 2-phthalimidoethylpyridinium *p*-toluenesulfonate (VIII) and bis(2-phthalimidoethyl) *o*-phthalate (IX) were isolated, originally as by-products and subsequently by direct synthesis. The former (VIII) was the major product if 2-phthalimidoethanol (I) was treated with pyridine and *p*-toluenesulfonyl chloride while the latter (IX) could be isolated if the tosylation of I containing traces of phthalic anhydride was accomplished in the absence of pyridine.



EXPERIMENTAL

2-Phthalimidoethyl acetate (II). Phthalic anhydride (148 g., 1 mole) and 300 ml. of benzene were stirred and heated just under reflux while adding 2-aminoethanol (61.9 g., 1.01 moles) dropwise. The water formed was removed with a phase-separating head during 20 hr. of refluxing. To the slightly cooled, clear solution was added 4 ml. of 95% sulfuric acid and a simple distillation head was substituted for the original head. Then, as 450 g. of acetic anhydride was added, the heat of the reaction was employed to distill the benzene. Distillation was continued with the application of heat until the temperature of the reaction mixture reached 150° and its volume was about 400 ml. Cooling overnight (5°) afforded crystals which were filtered, washed with water and dried. A single crystallization from ethanol-water afforded pure 2-phthalimidoethyl acetate; yield 202 g. (a further 8 g. could be recovered from the mother liquor for an over-all yield of 90%), m.p. 88.5–89.0° (lit.,[4] m.p. 88–89°).

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[4] W. E. Hanford and H. B. Stevenson, U. S. Patent 2,276,840 (1942).

If desired, the intermediate, 2-phthalimidoethanol (I), could be isolated by cooling the benzene solution (above); yield 190 g. (99%), m.p. 126–127° (lit.,[5] m.p. 126–127°).

Poly(vinylamine perchlorate) (VI). Following Hanford and Stevenson,[4] the 2-phthalimidoethyl acetate was passed through a packed tube heated at 570°. The *N*-vinyl-phthalimide (III) obtained, m.p. 85.5–86.5° (lit.,[4] m.p. 85–86°), in 75% yield was polymerized with dibenzoyl peroxide in methanol-1,2-dichloroethane (15/85, v/v) following the method of Reynolds and Kenyon.[3] The nearly quantitative yields of white, finely divided poly(*N*-vinylphthalimide) (IV) were treated with hydrazine following the method of Reynolds and Kenyon.[3] Thus, the polymer (120 g., 0.69 mole) was added in portions to 180 ml. of hydrazine hydrate (85%) stirred at 100° under nitrogen. After 24 hr., the solution was cooled, diluted with an equal volume of water, and steam-distilled until no additional hydrazine could be detected[6] in the distillate. After acidification to *p*H 4 with perchloric acid, the mixture was filtered and dialyzed against water. The dialyzate was concentrated under reduced pressure to 200 ml. and treated successively with three 100-ml. portions of Amberlite IRA-400 (OH^-) resin. The solution was adjusted to *p*H 3.0 with dilute perchloric acid. The solid product obtained on lyophilization contained less chlorine than calculated for the desired product. The denciency was determined by the analysis, and after dissolving the polymer in water, the required amount of perchloric acid (about 5% of the total) was added and the product was again recovered by lyophilization; yield 48 g. (49%) of light-brown, hygroscopic poly(vinylamine perchlorate) (VI); analytical sample dried under reduced pressure over sodium hydroxide.

Anal. Calcd. for $C_2H_5N \cdot HClO_4$: C, 16.74; H, 4.21; N, 9.76; Cl, 24.70. Found: C, 16.83; H, 4.29; N, 9.70; Cl, 24.95.

Properties of poly(vinylamine perchlorate). The molecular weight was determined by Dr. Quentin Van Winkle of the Department of Chemistry of The Ohio State University employing a B-S Light Scattering Photometer (Phoenix Precision Instrument Co., Philadelphia). From measurements in 0.1*M* sodium chloride a value of 90,000 was obtained. This molecular weight resulted from calculations employing the value of C/τ at infinite dilution as determined by the linear extrapolation of the data obtained at finite concentrations.

Poly(vinylamine perchlorate) is very soluble in water and ethanol, dissolves very slowly in acetone but not in ethyl acetate, benzene, or ether. On heating in a test tube, the salt melts and then explodes with a small flash of light leaving a small carbonaceous residue. The polymer also can be detonated by a firm hammer blow on a steel anvil but has been pulverized (caution) in small amounts with a mortar and pestle.

Bis(2-phthalimidoethyl) o-phthalate (IX). 2-Phthalimidoethanol (206 g., 1.08 mole), which had been purified by three wasteful recrystallizations from ethanol (95%), was dissolved in 1.5 l. of refluxing benzene containing 2 ml. of 95% sulfuric acid. Phthalic anhydride (80 g., 0.54 mole) was added in portions to the refluxing solution and the water formed (10 ml.) was removed with a phase-separating head during 20 hr. On cooling and diluting with an equal volume of absolute ethanol, crystals formed which were filtered, washed with water, and dried (110°); yield 220 g. (80%), m.p. 161–162°. The analytical sample (m.p. 164–165°) was obtained by a single crystallization from acetone-ethanol.

Anal. Calcd. for $C_{28}H_{20}N_2O_8$: C, 65.62; H, 3.93; N, 5.47; mol. wt., 512. Found: C, 65.68; H, 3.82; N, 5.43; mol. wt., 511 (Rast).

2-Phthalimidoethylpyridinium p-toluenesulfonate (VIII). 2-Phthalimidoethyl *p*-toluenesulfonate (VII) was prepared following the procedure of Peacock and Dutta[7] in 90% yield (m.p. 142–143°). This sulfonate (30 g.) was refluxed for 5 hr. with 150 ml. of dry pyridine and the solution on cooling deposited crystals (VIII) which were washed with ether and dried; yield 36.5 g. (99%), m.p. 205–206°.

Anal. Calcd. for $C_{22}H_{20}N_2O_5S$: C, 62.25; H, 4.75; N, 6.60; S, 7.55; neut. equiv., 424. Found: C, 62.31; H, 4.70; N, 6.64; S, 7.57; neut. equiv., 427.

The pyridinium compound (VIII) was originally isolated as the major product during an attempt to prepare the tosylate (VII) employing a mixture of pyridine and *p*-toluenesulfonyl chloride.

If the 2-phthalimidoethanol employed for the synthesis of the sulfonate derivatives was contaminated with phthalic anhydride, small amounts of the bis(2-phthalimidoethyl) *o*-phthalate could be isolated by pouring the crude pyridinium compound into water which left the phthalate as an insoluble residue. The phthalate derivative could also be recovered under similar circumstances from the mother liquors formed during the crystallization of the 2-phthalimidoethyl *p*-toluenesulfonate. The only way found to avoid the appearance of this contaminant in the sulfonate derivatives was to effect the condensation of the phthalic anhydride with a slight excess of the 2-aminoethanol.

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[5] S. Gabriel, *Ber.*, 21, 566 (1888).

[6] F. Feigl, *Spot Tests in Organic Analysis*, 5th English Ed., Elsevier, New York, 1956, p. 297.

[7] D. H. Peacock and U. C. Dutta, *J. Chem. Soc.*, 1303 (1934).

Glycyliminodiacetic Acid

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The literature contains few examples of peptides of an imino acid other than those derived from proline. Attempts in this laboratory to prepare β-alanyliminodipropionic acid[2] and α-alanyliminodiacetic acid[3] were unsuccessful, but the simplest member of the series, glycyliminodiacetic acid, $NH_2CH_2CON(CH_2COOH)_2$, has now been obtained.

The conversion of carbobenzoxyglycinehydrazide[4] to the azide and the coupling of the latter with the dimethyl ester of iminodiacetic acid[5] gave a syrup, which was saponified to the crystalline carbobenzoxyglycyliminodiacetic acid. Hydrogenolysis produced glycyliminodiacetic acid.

Possible by-products of the azide coupling are derivatives of the isocyanate resulting from a Curtius rearrangement of the azide. For example, Nyman and Herbst,[6] in attempting to condense the azide of carbobenzoxy-L-valine hydrazide with L-valine ethyl ester, obtained the substituted urea, formed by interaction of the isocyanate with the valine ester. A similar substituted urea was ap-

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[1] From the M.S. thesis of Shirley Shyluk, University of Delaware, 1958.

[2] G. L. Ford, M.S. thesis, University of Delaware, 1951.

[3] T. E. Majewski, M.S. thesis, University of Delaware, 1953.

[4] S. Simmonds, J. I. Harris, and J. S. Fruton, *J. Biol. Chem.*, 188, 259 (1951).

[5] J. V. Dubsky, *Ber.*, 50, 1694 (1917).

[6] M. A. Nyman and R. M. Herbst, *J. Org. Chem.*, 15, 117 (1950).