then taken up in ether, the ethereal solution washed with a few ml. of water and dried over sodium sulfate, the ether distilled, and the residue vacuum-fractionated. The following isocyanates were obtained, as colorless, pleasant-smelling oils:

*α,α-dimethyl-β-m-xylylethyl isocyanate* (46% yield), b.p. 151–152°/20 mm., $n_D^{22}$ 1.5158.

*Anal.* Calcd. for $C_{13}H_{17}NO$: N, 6.9. Found: N, 6.5.

*α,α-dimethyl-β-p-xylylethyl isocyanate* (51% yield), b.p. 149–151°/20 mm., $n_D^{22}$ 1.5172.

*Anal.* Calcd. for $C_{13}H_{17}NO$: N, 6.9. Found: N, 6.6.

*α,α-dimethyl-β-(p-propylphenyl)ethyl isocyanate* (47% yield), b.p. 145–147°/13 mm., $n_D^{22}$ 1.5108.

*Anal.* Calcd. for $C_{14}H_{19}NO$: N, 6.5. Found: N, 6.2.

*α,α-dimethyl-β-(2,4,6-trimethylphenyl)ethyl isocyanate* (49% yield), b.p. 146–149°/13 mm.

*Anal.* Calcd. for $C_{14}H_{19}NO$: N, 6.5. Found: N, 6.2.

*Hydrolysis of the isocyanates.* The isocyanates (0.1 mole) were hydrolyzed by stirring on a water bath with a large excess of concd. hydrochloric acid (400 ml.), the reaction being manifest by a more or less rapid evolution of carbon dioxide. When this had terminated, the mixture was boiled until a totally limpid liquid was obtained; on cooling, water (250 ml.) was added, the liquid was made basic with 30% aqueous sodium hydroxide, and the reaction product was taken up immediately in ether. The ethereal solution was then washed with a minimum of water and dried over sodium sulfate, the solvent was removed, and the residue was vacuum-fractionated. The yields ranged from 30 to 88%. The following amines were obtained, as colorless oils, together with their hydrochlorides (prepared by saturating with hydrogen chloride a solution of the amine in ether, and crystallization of the precipitate from ethanol + benzene):

*α,α-dimethyl-β-(2,4-dimethylphenethyl)amine* (IV), b.p. 132–133°/22 mm., $n_D^{20}$ 1.5231.

*Anal.* Calcd. for $C_{12}H_{19}N$: C, 81.3; H, 10.8; N, 7.9. Found: C, 81.3; H, 10.6; N, 7.9.

*Hydrochloride*, colorless needles, m.p. 209° (sublimation above 170°).

*Anal.* Calcd. for $C_{12}H_{20}ClN$: Cl, 16.6; N, 6.6. Found: Cl, 16.8; 6.8.

*α,α-dimethyl-β-(2,5-dimethylphenethyl)amine* (V), b.p. 118°/15 mm., $n_D^{21.5}$ 1.5246.

*Anal.* Calcd. for $C_{12}H_{19}N$: C, 81.3; H, 10.8; N, 7.9. Found: C, 81.3; H, 10.8; N, 7.9.

*Hydrochloride*, m.p. 230°.

*Anal.* Calcd. for $C_{12}H_{20}ClN$: Cl, 16.6; N, 6.6. Found: Cl, 16.5; N, 6.4.

*α,α-dimethyl-β-p-propylphenethylamine* (VI), b.p. 123–125°/14 mm., $n_D^{22}$ 1.5182.

*Anal.* Calcd. for $C_{13}H_{21}N$: C, 81.6; H, 11.1; N, 7.3. Found: C, 81.4; H, 10.9; N, 7.1.

*Hydrochloride*, m.p. 217° (sublimation above 166°).

*Anal.* Calcd. for $C_{13}H_{22}ClN$: Cl, 15.6; N, 6.2. Found: Cl, 15.5; N, 6.0.

*α,α-dimethyl-β-(2,4,6-trimethylphenethyl)amine* (VII), b.p. 130–131°/14 mm.

*Anal.* Calcd. for $C_{13}H_{21}N$: C, 81.6; H, 11.1; N, 7.3. Found: C, 81.6; H, 10.9; N, 7.2.

*Hydrochloride*, m.p. 214° (sublimation above 175°).

*Anal.* Calcd. for $C_{13}H_{22}ClN$: Cl, 15.6; N, 6.2. Found: Cl, 15.8; N, 5.9.

*N,N'(α,α-dimethyl-β-o-chlorophenethyl)urea* (VIII). This compound was obtained as the sole product from the hydrolysis of the corresponding isocyanate, and crystallized from benzene in shiny colorless prisms, m.p. 224°.

*Anal.* Calcd. for $C_{21}H_{26}Cl_2N_2$: C, 64.1; H, 6.7; N, 7.1. Found: C, 64.1; H, 6.8; N, 7.0.

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PARIS (V^e), FRANCE

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[CONTRIBUTION FROM THE ORGANIC CHEMICALS DIVISION, ST. LOUIS RESEARCH DEPARTMENT, MONSANTO CHEMICAL CO.]

# *N*-Substituted Glycinate and Alaninate Esters

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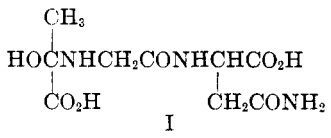
*N*-Substituted glycinate and α- and β-alaninate esters were prepared as possible antimetabolites for the control of *Fusarium* wilt diseases. Some qualitative results are presented on the relative ease of displacement of the α-halogen atom and aminolysis of the ester group in the reaction of haloacetate esters with primary aliphatic amines.

The pathogenicity of *Fusarium lycopersici* has been attributed to one of its metabolic products, lycomarasmin (I). Tomato wilt, an important economic plant disease, is caused by this organism. The toxic effects of I are also reproduced by the synthetic peptide serylglycylasparatic acid and reversed by serylglycylglutamic acid.[1]



I

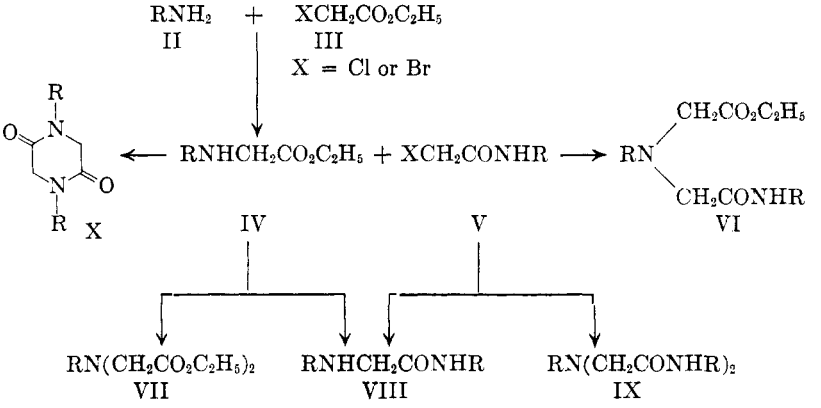
Since lycomarasmin is a tripeptide composed of asparagine, glycine, and α-hydroxyalanine units, it was felt that antimetabolites for the control of wilt diseases[2] might be found in *N*-substituted glycinates and alaninates. These amino acid derivatives might prevent the formation of the toxic agent, lycomarasmin. Growth inhibition of the fungus would also result if the biosynthesis of the tripeptide were essential to the *Fusarium* organism.

*N*-Substituted glycinates have been prepared by the alkylation of amines with haloacetates,[3] by reductive alkylation of aldehydes and ketones with

(1) J. W. Foster, *Chemical Activities of Fungi*, Academic Press Inc., New York, N. Y., 1949, p. 494.

(2) *Plant Diseases, The Year Book of Agriculture*, U. S. Dept. of Agriculture, Washington, D. C., 1953.

glycine,[4] by a modified Strecker synthesis,[5] and by alkylation of glycine with dialkyl sulfates.[6] Since our interest was mainly the preparation of *N*-monosubstituted glycinates (IV), a study of only the first of these methods was undertaken. Because of the numerous side reactions resulting from competitive reactions involving the displacement of the α-halogen atom and aminolysis of the ester group, yields of IV are about 50%. The yields or isolation of by-products such as VII–IX have not been reported by previous investigators.[3,7,8]




In the present study of the reaction of allyl-, butyl- and benzyl-amine with ethyl chloro- and bromoacetate, compounds of the type IV, VII–IX have been isolated. *N,N*-Disubstituted 2,5-diketopiperazines (X)[4a] were not isolated from among the reaction products but were formed in small amounts (*ca.* 5%) during storage of samples of IV for several months.

Allylamine and ethyl chloroacetate in ether at 0–5° gave only a 7% yield of ethyl *N*-allylglycinate (IVa) and a 72% yield of *N,N'*-diallylglycinamide (VIIIa). However, allylamine and ethyl bromoacetate, under the same conditions, gave a 75% yield of the alkylated product IVa. Butylamine and ethyl chloroacetate in refluxing benzene gave rise to three products: ethyl *N*-butylglycinate (IVb) in 12.5% yield, *N,N'*-dibutylglycinamide (VIIIb) in 50% yield and butylimino-bis-*N*-butylacetamide (IXb) in 26% yield. Ethyl bromoacetate and butylamine gave a 71% yield of IVb and a 16% yield of diethyl butyliminodiacetate (VIIIb). Finally, benzylamine and ethyl chloracetate in refluxing benzene gave rise to a 61.5% yield of ethyl *N*-benzylglycinate (IVc) and only 10% yield of *N,N'*-dibenzyl glycinamide (VIIIc).

The course of reaction of allyl- and butylamine with ethyl chloro- and bromoacetate is clearly shown to be governed by the difference in lability of the halogen atoms. Aminolysis of the ester group and chloride displacement must have proceeded at about the same rate to account for the yields of products. If displacement proceeded much faster than aminolysis, at least a 50% yield of IVa or IVb should have been realized, based on the mole ratio of reactants used.

The effect of the nature of an electronegative α-substituent on the rate of aminolysis of aliphatic esters has been strikingly shown by Audrieth and Kleinberg.[9] Ethyl cyanoacetate afforded 96–100% yields of cyanoacetamide whereas ethyl acetate gave only 0–3% yields of amide under identical conditions.

It is interesting to compare the action of benzylamine with ethyl chloroacetate and butyl chloroacetate to give the respective glycine esters. The two reactions were performed similarly except that, in the former, the mixture was refluxed (79°) for one hour and, in the latter, it was held for four hours at 40–48°. The yield of glycinate ester was 61.5% for the ethyl ester and 31% for the butyl

(3) (a) R. Alpern and C. Weizmann, *J. Chem. Soc.*, 84 (1911). (b) J. Fugger, J. M. Tien, and I. M. Hunsberger, *J. Am. Chem. Soc.* **77**, 1843 (1955). (c) A. T. Mason and G. R. Winder, *J. Chem. Soc.*, 18 (1894). (d) C. Paal and E. Weidenkaff, *Ber.*, **39**, 81 (1906). (e) R. Willstatter, *Ber.*, **35**, 584 (1902). (f) W. Voss and H. Wulkan, *Ber.*, **70**, 388 (1937).

(4) (a) L. Bilek, J. Derkosch, H. Michl, and F. Wessely, *Monatsh*, **84**, 717 (1953). (b) R. E. Bowman and H. H. Stroud, *J. Chem. Soc.*, 1342 (1950). (c) R. E. Bowman, *J. Chem. Soc.*, 1346 (1950).

(5) (a) L. W. Ziemlak, J. L. Bullock, F. C. Bersworth, and A. E. Martell, *J. Org. Chem.*, **15**, 255 (1950). (b) S. M. McElvain and P. M. Laughton, *J. Am. Chem. Soc.*, **73**, 448 (1951). (c) C. E. Dalgliesch and F. G. Mann, *J. Chem. Soc.*, 658 (1947). (d) D. B. Luten, Jr., *J. Org. Chem.*, **3**, 588 (1939). (e) A. H. Cook and S. F. Cox, *J. Chem. Soc.*, 2334 (1949). (f) R. A. Jacobson, *J. Am. Chem. Soc.*, **67**, 1996 (1945).

(6) J. Novak, *Ber.*, **45**, 834 (1912).

(7) W. V. Drake and S. M. McElvain, *J. Am. Chem. Soc.*, **56**, 697, 1810 (1934).

(8) J. A. King and F. H. McMillan, *J. Am. Chem. Soc.*, **72**, 1236 (1950).

(9) L. F. Audrieth and J. Kleinberg, *J. Org. Chem.*, **3**, 312 (1938).

TABLE I

ETHYL *N*-SUBSTITUTED GLYCINATES

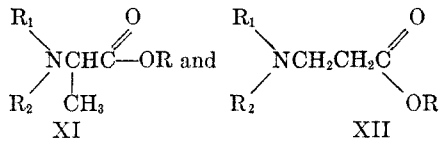
$R{\cdot}NHCH_2CO_2R'$

| R | R′ | Method | Yield, % | B.P. | Mm. Hg | $n_D^{25}$ | Carbon, % Calcd. | Carbon, % Found | Hydrogen, % Calcd. | Hydrogen, % Found | Nitrogen, % Calcd. | Nitrogen, % Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *i*-$C_3H_7$ | $C_2H_5$ | B | 39 | 46 | 4.0 | 1.4161 | — | — | — | — | 9.65 | 9.64 |
| *t*-$C_4H_9$ | $C_2H_5$ | B | 57 | 67 | 12.0 | 1.4206 | — | — | — | — | 8.80 | 8.74 |
| *n*-$C_{12}H_{25}$ | $C_2H_5$ | A | 46 | 160 | 2.7 | 1.4422 | 70.80 | 70.60 | 12.25 | 12.24 | 5.16 | 5.16 |
| $CH_2{=}C(CH_3)CH_2$[a] | $C_2H_5$ | A | 65 | 76 | 10.0 | 1.4384 | 61.12 | 60.74 | 9.62 | 9.64 | 8.26 | 8.31 |
| $(C_2H_5)_2NCH_2CH_2$ | $C_2H_5$ | B | 45 | 78 | 1.1 | 1.4410 | 59.37 | 59.24 | 10.96 | 10.77 | 13.25 | 13.44 |
| $CH_3O(CH_2)_3$ | $C_2H_5$ | A | 70 | 63 | 0.6 | 1.4312 | — | — | — | — | 8.09 | 8.09 |
| $C_2H_5O(CH_2)_3$ | $C_2H_5$ | B | 57 | 75 | 0.5 | 1.4309 | — | — | — | — | 7.40 | 7.50 |
| $C_6H_5CH(CH_3)$[b] | $C_2H_5$ | A | 59 | 85 | 0.25 | 1.5010 | — | — | — | — | 6.76 | 6.89 |
| $2,4\text{-}Cl_2C_6H_3CH_2$[d] | $C_2H_5$ | A | 54 | 140 | 0.8 | 1.5342 | — | — | — | — | 27.05[c] | 27.10 |
| $3,4\text{-}Cl_2C_6H_3CH_2$[e] | $C_2H_5$ | A | 44 | 132 | 0.35 | 1.5327 | — | — | — | — | 27.05[c] | 27.93 |
| $C_2H_5$ | $CH_2{=}CH{-}CH_2$ | A | 36 | 75 | 16.0 | 1.4357 | 58.72 | 58.18 | 9.15 | 9.11 | 9.78 | 9.49 |
| $CH_2{=}CH{-}CH_2$ | $CH_2{=}CH{-}CH_2$ | A | 50 | 89 | 13.0 | 1.4524 | 61.92 | 61.63 | 8.44 | 8.48 | — | — |
| $C_6H_5CH_2$ | $CH_2{=}CH{-}CH_2$ | A | 57 | 127 | 1.6 | 1.5142 | 70.22 | 70.08 | 7.37 | 7.29 | 6.83 | 6.77 |
| $CH_2{=}CH{-}CH_2$[f] | $C_4H_9$ | A | 58 | 95 | 10.0 | 1.4383 | 63.12 | 63.22 | 10.01 | 9.97 | 8.18 | 8.24 |
| $C_6H_5CH_2$[g] | $C_4H_9$ | A | 27 | 135 | 2.0 | 1.4962 | 70.56 | 70.49 | 8.65 | 8.74 | 6.33 | 6.52 |
| $CH_2{=}CH{-}CH_2$[h] | $C_{12}H_{25}$ | B | 50 | 162 | 2.0 | 1.4508 | — | — | — | — | 4.94 | 4.79 |
| $C_6H_5CH_2$ | $C_{12}H_{25}$ | B | 88 | — | — | 1.4856 | — | — | — | — | 4.20 | 3.97 |

[a] *Picrate:* m.p. 77–78°. *Anal.* Calcd. for $C_{14}H_{18}N_4O_9$: C, 43.52; H, 4.70; N, 14.49. Found: C, 43.97; H, 5.01; N, 14.70. [b] *Hydrochloride:* m.p. 151–152°. *Anal.* Calcd. for $C_{12}H_{17}NO_2{\cdot}HCl$: Cl, 15.20. Found: Cl, 15.36. [c] Chlorine analysis. [d] *Hydrochloride:* m.p. 159–160°. *Anal.* Calcd. for $C_{11}H_{13}Cl_2NO_2{\cdot}HCl$: Cl, 35.63. Found: 35.64. [e] *Hydrochloride:* m.p. 206–207°. *Anal.* Calcd. for $C_{11}H_{13}Cl_2NO_2{\cdot}HCl$: Cl, 35.63. Found: Cl, 35.62. [f] *Picrate:* m.p. 94–95°. *Anal.* Calcd. for $C_{15}H_{20}N_4O_9$: C, 45.00; H, 5.04; N, 13.99. Found: C, 45.50; H, 5.17; N, 13.77. [g] *Hydrochloride:* m.p. 102–103°. *Anal.* Calcd. for $C_{13}H_{19}NO_2{\cdot}HCl$: N, 5.43; Cl, 13.75. Found: N, 5.45; Cl, 13.73. (N. L. Drake and S. Melamed, U. S. Patent **2,653,895.**) [h] *Hydrochloride:* m.p. 97–98°. *Anal.* Calcd. for $C_{17}H_{33}NO_2{\cdot}HCl$: N, 4.38; Cl, 11.07. Found: N, 4.19; Cl, 11.26.

TABLE II

*N*-SUBSTITUTED ALANINATE ESTERS



XI XII

| XI or XII | R | $R_1$ | $R_2$ | Yield, % | B.P. | Mm. | $n_D^{25}$ | Nitrogen Analysis Calcd. | Nitrogen Analysis Found |
|---|---|---|---|---|---|---|---|---|---|
| XI | $C_2H_5$[a] | H | $CH_2{=}CH{-}CH_2$ | 41 | 68 | 11.0 | 1.4310 | 8.91 | 9.17 |
| XI | $C_2H_5$ | | $-CH_2CH_2-$ | — | 32 | 1.0 | 1.4276 | 9.78 | 9.96 |
| XII | $C_2H_5$ | | $-CH_2CH_2-$ | 88 | 75 | 13.0 | 1.4326 | 9.78 | 9.96 |
| XII | $C_4H_9$ | | $-CH_2CH_2-$ | 88 | 85 | 4.5 | 1.4362 | 8.18 | 8.13 |
| XII | $CH_3OCH_2CH_2$ | | $-CH_2CH_2-$ | 89 | 82 | 1.3 | 1.4432 | 8.09 | 8.19 |
| XII | $C_2H_5$[b] | H | $CH_2{=}CHCH_2$ | 80 | 56 | 1.2 | 1.4390 | 8.52 | 8.91 |

[a] *Hydrochloride:* m.p. 95–96°. *Anal.* Calcd. for $C_8H_{15}NO_2{\cdot}HCl$: N, 7.23; Cl, 18.31. Found: N, 7.00; Cl, 18.36. [b] *Hydrochloride:* m.p. 82–83°. *Anal.* Calcd. for $C_8H_{15}NO_2{\cdot}HCl$: Cl, 18.32. Found Cl, 18.38.

ester. The butyl ester reaction gave a large high-boiling residue.

In contrast to the action of allylamine, diallylamine was ineffective in the aminolysis of ethyl chloroacetate. This reaction was performed in the presence of 8.4 mole percent of diallylamine hydrochloride in ethanol in the hope of catalyzing the aminolysis[10] of the ester group. The only product isolated was ethyl *N,N*-diallylglycinate.

In an attempt to repress side reactions in the preparation of glycinates of types IV, bases other than excess amine were studied. Triethylamine was used successfully in place of one mole excess of primary amine, but the yields in general were of the same order. The use of sodium carbonate and sodium acetate[11] lead to the isolation of over 50% yields of dialkylated products VII.

Tars were formed when either sodium hydroxide or a large excess of primary amine were used as the hydrogen halide scavengers.

(10) P. K. Glasoe and L. F. Audrieth, *J. Org. Chem.*, **4**, 54 (1939); P. K. Glasoe, J. Kleinberg, and L. F. Audrieth, *J. Am. Chem. Soc.*, **61**, 2387 (1939).

(11) (a) W. Baker, W. D. Ollis, and V. D. Poole, *J. Chem. Soc.*, 307 (1949). (b) F. E. King and J. W. Clark-Lewis, *J. Chem. Soc.*, 3080 (1951). (c) P. L. Southwick, H. L. Dimond, and R. E. Stansfield, *J. Am. Chem. Soc.*, **78**, 1608 (1956). (d) C. G. Schwalbe, W. Schulz, and H. Jochheim, *Ber.*, **41**, 3790 (1908).

The glycinates prepared during the course of this work and not reported previously are listed in Table I. α-(*N*-Substituted) alaninate esters were prepared from the α-bromoesters according to the procedure used for the glycinates. The β-alaninates were prepared by 1,4- addition of the amine to the appropriate acrylic ester. These new compounds are listed in Table II.

The fungicidal activities of the glycinates and alaninates are presented in Table III. Only the ethyl *N*-allyl- and *N*-benzylglycinates, their hydrochlorides, and the picrate of the benzyl derivative possessed activity. Modification of the ester grouping of *N*-allyl and *N*-benzyl glycinates resulted in a total loss in activity with the exception of allyl *N*-allylglycinate. Similarly, the ethyl α- or β-*N*-allylalaninates were without activity in these tests. From these results, it is apparent that the structural requirements for systemic fungicidal activity in the glycinate series are highly specific.

TABLE III

SYSTEMIC FUNGICIDAL ACTIVITY[a] OF *N*-SUBSTITUTED GLYCINATES AND ALANINATES

| $RNHCH_2COOC_2H_5$ | | Activity Rating[b] |
|---|---|---|
| $i$-$C_3H_7$ | | N |
| $CH_2$=$CHCH_2$ | | E |
| $CH_2$=$CHCH_2$·HCl | | E |
| $t$-$C_4H_9$ | | N |
| $CH_2$=$CH(CH_3)CH_2$ | | N |
| $(C_2H_5)_2NCH_2CH_2$— | | N |
| $CH_3O(CH_2)_3$— | | N |
| $C_2H_5O(CH_2)_3$— | | N |
| $C_6H_5$—$CH(CH_3)$ | | N |
| $C_6H_5CH_2$— | | E |
| $C_6H_5CH_2$—·HCl | | E |
| $C_6H_5CH_2$—·picrate | | E |
| 2,4-$Cl_2C_6H_3CH_2$— | | N |
| 3,4-$Cl_2C_6H_3CH_2$— | | N |
| $RNHCH_2COOR'$ | | |
| R | R′ | |
| $C_2H_5$ | $CH_2$=$CH$—$CH_2$— | N |
| $CH_2$=$CHCH_2$ | $CH_2$=$CH$—$CH_2$— | P |
| $C_6H_5CH_2$— | $CH_2$=$CHCH_2$— | N |
| $CH_2$=$CHCH_2$ | $C_4H_9$ | N |
| $C_6H_5CH_2$— | $C_4H_9$ | N |
| $CH_2$=$CHCH_2$ | $n$-$C_{12}H_{25}$ | N |
| $C_6H_5CH_2$— | $n$-$C_{12}H_{25}$ | N |
| $RNHCH_2CH_2COOR'$ | | |
| R | R′ | |
| $CH_2$=$CHCH_2$— | $C_2H_5$ | N |
| $RNH$—$\underset{\displaystyle CH_3}{\underset{\vert}{CH}}$—$COOR'$ | | |
| R | R′ | |
| $CH_2$=$CHCH_2$— | $C_2H_5$ | N |

[a] The systemic test for the control of *Fusarium oxysporum* f-*lycopersici* in tomatoes is a modification of that by A. E. Dimond, *et al.*, *Connecticut Agr. Expt. Sta. Bull.*, 557 (1952). Chemicals were applied as foliage sprays at a concentration of 2500 p.p.m. rather than by the root soaking technique of Dimond. [b] N = no good; heavy vascular discoloration. P = promising; slight vascular discoloration. E = excellent; no vascular discoloration.

## EXPERIMENTAL[12]

*Glycinate esters.* The method used for ethyl *N*-methallylglycinate is representative.

A solution of 21.3 g. (0.3 mole) of methallylamine, 30 g. (0.3 mole) of triethylamine and 200 ml. of ether or benzene was cooled to 0–5°. A solution of 47.5 g. (0.3 mole) of ethyl bromoacetate in 100 ml. of ether or benzene was added in 2.5 hr. at 0–5°. The mixture was allowed to warm to room temperature and stirred overnight. The triethylamine hydrobromide (92.5% recovery) was removed by filtration. After removal of the solvent, the product was distilled *in vacuo*. This procedure is designated as A in Table I; in procedure B, 2 equivalents of amine were used and triethylamine was omitted.

When anhydrous sodium carbonate was used in place of triethylamine as a hydrogen bromide scavenger only iminodiacetates were isolated. To a suspension of 53 g. (0.5 mole) of sodium carbonate and 29.6 g. (0.5 mole) of propylamine in 200 ml. of dry benzene, 83.5 g. (0.5 mole) of ethyl bromoacetate was added over about 2 hr. at 20–25°. The mixture was stirred overnight and the inorganic salts filtered. The solvent was removed and diethyl *N*-propyliminodiacetate was isolated in 77% yield; b.p. 127° (10 mm.), $n_D^{25}$ 1.4346.

*Anal.* Calcd. for $C_{11}H_{21}NO_4$: N, 6.06. Found: N, 6.03.

The picrate was prepared in ethanol and recrystallized from hexane–ethyl acetate mixture; m.p. 83–84°.

*Anal.* Calcd. for $C_{17}H_{24}N_4O_{11}$: C, 44.23; H, 5.25; N, 12.14. Found: C, 44.24; H, 5.43; N, 12.10.

*Diallyl N-ethyliminodiacetate* was prepared similarly in 51.8% yield; b.p. 110° (0.9 mm.), $n_D^{25}$ 1.4160.

*Anal.* Calcd. for $C_{12}H_{19}NO_4$: N, 6.07. Found: N, 6.05.

*Diethyl N-ethylimidodiacetate* was prepared in a similar manner in 45.5% yield. This compound was also formed in 54.8% yield when sodium acetate was used in place of carbonate; b.p. 113–115° (5.3 mm.), $n_D^{25}$ 1.4247.

*Anal.* Calcd. for $C_{10}H_{19}NO_4$: N, 6.45. Found: N, 6.25.

*Alaninate esters.* The α-*N*-substituted alaninate esters were prepared according to Procedure A above. The β-*N*-substituted alaninate esters were prepared from the acrylate ester and amine as shown by this typical example for *butyl 1-aziridinepropionate.* Ethylenimine (12.9 g., 0.3 mole) was added to 38.4 g. (0.3 mole) of butyl acrylate at 20° during 0.5 hr. The reaction temperature was allowed to rise to 25–40° and held overnight. The aziridinepropionate was isolated by direct distillation. In some instances, absolute ethanol (100 ml./0.1 mole) was used as solvent.

Treatment of butyl 1-aziridinepropionate with anhydrous hydrogen chloride[13] in ether gave a 60% yield of *butyl S-(2-chloroethylamino)propionate hydrochloride*, m.p. 138–139°.

*Anal.* Calcd. for $C_9H_{18}ClNO_2$·HCl: ionic Cl, 14.52; total Cl, 29.34. Found: ionic Cl, 14.65; total Cl, 29.34.

*Alkylation of amines.* A. *Allylamine.* (1). *Ethyl chloroacetate.* A solution of 142 g. (2.5 moles) of allylamine and 122 g. (1.0 mole) of ethylchloroacetate in 300 ml. of ether was stirred at 0–5° for 5 hr., and allowed to stand at room temperature over the week-end. The ether layer was separated and the lower layer was extracted with ether and benzene. The solvents were combined, removed *in vacuo*, and the residue distilled. Two fractions were collected: Fraction I, b.p. 71–105° (8 mm.), $n_D^{25}$ 1.4361; 10 g. (7% yield). Fraction II, b.p. 110–135° (2 mm.), $n_D^{25}$ 1.4852 (15% yield).

Fraction I consisted chiefly of ethyl *N*-allylglycinate[3a] as shown by conversion to its hydrochloride; m.p. 115–116°.

*Anal.* Calcd. for $C_7H_{13}NO_2$·HCl: Cl, 19.74. Found: Cl, 19.84.

Fraction II was identified as *N,N′*-diallyl glycinamide by conversion to its hydrochloride; m.p. 128–129°.

*Anal.* Calcd. for $C_8H_{14}N_2O$·HCl: C, 50.39; H, 7.93; Cl, 18.59. Found: C, 50.25; H, 8.01; Cl, 18.70.

(12) We are indebted to A. Bybell, O. S. Kring, and J. L. O'Sullivan for the analyses.

(13) H. Bestian, *Ann.*, 566, 210 (1950).

The lower layer, after extraction with ether and benzene, was dissolved in chloroform and neutralized with sodium hydroxide. Separation and evaporation of the chloroform left 70 g. (57% yield) of *N,N'*-diallylglycinamide. The hydrochloride melted at 127–128°. A mixture melting point with the hydrochloride of Fraction II was not depressed.

(2). Ethyl bromoacetate. A solution of 114 g. (2.0 moles) of allylamine and 167 g. (1.0 mole) of ethyl bromoacetate in 500 ml. of ether was stirred at 5–10° during 3 hr. and then overnight at room temperature. Allylamine hydrobromide (97% recovery) was collected on a filter. The solvent was removed and the residue distilled to give 104 g. (73% yield) of ethyl *N*-allyl glycinate [b.p. 88–89° (30 mm.), $n_D^{25}$ 1.4351]. The hydrochloride melted at 115–116° and was shown to be identical with that from Fraction I above by mixture melting point.

B. *Butylamine.* (1). *Ethyl chloroacetate.* A solution of 168 g. (2.3 moles) of butylamine in 1 l. of benzene was treated with 122 g. (1.0 mole) of ethyl chloroacetate at 25–30° during 1 hr. The solution was heated at reflux for 2 hr. Butylamine hydrochloride did not precipitate during the reaction period. The solution was made alkaline with sodium hydroxide and the organic layer was separated. The residue after removal of the solvent was distilled and yielded two fractions: Fraction I, b.p. 87–93° (15.5 mm.), $n_D^{25}$ 1.4240, 15.5 g. (12.5% yield); Fraction II, b.p. 121–127° (0.55 mm.), $n_D^{25}$ 1.4551, 75.5 g. (50% yield).

Fraction I consisted chiefly of ethyl *N*-butylglycinate as shown by conversion to its hydrochloride: m.p. 186–187°.

*Anal.* Calcd. for $C_8H_{17}NO_2 \cdot HCl$: C, 49.10; H, 9.27; Cl, 18.14; N, 7.15. Found: C, 49.16; H, 9.36; Cl, 18.38; N, 7.11.

Fraction II was shown to be *N,N'*-dibutyl glycinamide by conversion to its hydrochloride; m.p. 172–173°.

*Anal.* Calcd. for $C_{10}H_{22}N_2O \cdot HCl$: C, 53.98; H, 10.35; Cl, 15.95; N, 12.60. Found: C, 53.84; H, 10.45; Cl, 16.02; N, 12.62.

The residue (46.5 g., 26% yield) which remained after distillation of Fraction I and II consisted of butyliminobis(*N*-butylacetamide) which was converted to its hydrochloride, m.p. 95–96°.

*Anal.* Calcd. for $C_{16}H_{33}N_3O_2 \cdot HCl$: C, 57.09; H, 10.20; Cl, 10.56; N, 12.52. Found: C, 56.60; H, 10.46; Cl, 10.62; N, 12.19.

Ethyl *N*-butylglycinate is reported[14] to have been prepared in 56.5% yield [b.p. 174–175° (20 mm.), $n_D^{25}$ 1.4600] from ethyl chloroacetate and butylamine. The compound is undoubtedly *N,N'*-dibutylglycinamide.

(2). *Ethyl bromoacetate.* When butylamine was treated with ethyl bromoacetate according to the procedure as given for ethyl chloroacetate, a 94% recovery of butylamine hydrobromide was realized. There was obtained a 71% yield of ethyl *N*-butylglycinate [b.p. 52° (1.1 mm.), $n_D^{25}$ 1.4236] and a 16% yield of diethylbutyliminodiacetate [b.p. 100–105° (1.1 mm.), $n_D^{25}$ 1.4350], whose picrate melted at 94–95°. The hydrochloride formed as an oil.

*Anal.* Calcd. for $C_{18}H_{26}N_4O_{11}$: C, 45.59; H, 5.51; N, 11.81. Found: C, 45.82; H, 5.70; N, 11.60.

The above method of preparation is essentially that of Fugger, Tien, and Hunsberger[3b] but the iminodiacetate was not reported.

C. *Benzylamine.* Treatment of benzylamine with ethyl chloroacetate, as in the alkylation of butylamine, afforded a 61% yield of ethyl *N*-benzylglycinate[15]; b.p. 106° (0.9 mm.); $n_D^{25}$ 1.5041 (picrate, m.p. 166–168°).

The residue from the distillation was dissolved in ethyl acetate, filtered, and saturated with hydrogen chloride. There was obtained about 10% yield of the *N,N'*-dibenzylglycinamide hydrochloride, m.p. 244–245°.

*Anal.* Calcd. for $C_{16}H_{18}N_2O \cdot HCl$: C, 66.09; H, 6.59; Cl, 12.20; N, 9.65. Found: C, 66.58; H, 6.77; Cl, 12.34; N, 9.55.

D. *Diallylamine.* To 200 ml. of absolute ethanol containing 0.042 mole of hydrogen chloride, there was added 48.5 g. (0.5 mole) of diallylamine and 61 g. (0.5 mole) of ethyl chloroacetate. The mixture was held at 1–2° for 18 hr. and then at 24° for 24.5 hr. Samples were removed periodically and titrated for amine and chloride ion. The increase in chloride ion and decrease in amine concentrations were proportional at both temperatures and reached constant values of 0.25 mole each. Thus, aminolysis of the ester group was negligible. Alkylation was the predominant reaction. At the end of the reaction period, the mixture was poured into water and extracted with ether. There was obtained 0.19 mole (38% recovery) of ethyl chloroacetate, and 0.17 mole (68% yield on ester consumed) of ethyl *N,N*-diallylglycinate, b.p. 112–114° (0.35 mm.), $n_D^{25}$ 1.4448, neut. equiv. 184 (theory neut. equiv. 183).

Saponification of the diallyl glycinate with 20% potassium hydroxide at reflux for 2 hr. afforded a 65% yield of *N,N*-diallylglycine, m.p. 109–110°. The melting point was not depressed on admixture with an authentic sample (m.p. 109–110°) prepared from diallylamine and chloroacetic acid.

*Anal.* Calcd. for $C_8H_{13}NO_2$: N, 9.02. Found: N, 9.19.

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