Nitrophthaloyl and Aminophthaloyl Derivatives of Amino Acids

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Seventeen 3-nitrophthalimido acids, 18 4-nitrophthalimido acids, 14 3-aminophthalimido acids, and 14 4-aminophthalimido acids have been prepared.

A RECENT paper (*3*) described the preparation and some of the properties of the nitrophthaloyl and aminophthaloyl derivatives of glycine. This work has been extended to the preparation of the nitrophthaloyl and aminophthaloyl derivatives of a number of other amino acids. Although it gives excellent results with glycine, the use of nitrobenzene as a solvent for nitrophthaloylations was unsatisfactory with other amino acids. The phthaloylation method of Billman and Harting (*2*) gave satisfactory nitrophthaloylations in most cases. The nitrophthalic acids were as effective as their anhydrides in achieving nitrophthaloylation by this method. The aminophthaloyl derivatives were prepared by hydrogenation of the nitrophthaloyl derivatives.

EXPERIMENTAL

Nitrophthaloyl Derivatives of Amino Acids. Intimate mixtures of 0.01 mole of an amino acid with 0.01 mole of a nitrophthalic acid or anhydride were fused according to the method of Billman and Harting (*2*). The products were recrystallized until no further improvement in melting points resulted. The experimental data are summarized in Table I. The products are all ivory to cream-colored powders.

Table I. Nitrophthaloyl Derivatives of Amino Acids[a]

Amino Acid	Position of Nitro Group	Yield, %	Recrystallized from	M.P., ° C.[b]
DL-Alanine	3	75	50% Ethanol	165–7
DL-Alanine	4	76	70% Ethanol	161.5–3.5
β-Alanine	3	83	70% Ethanol	145–6[c]
β-Alanine	4	65	Water	209–10[d]
DL-α-Amino-*n*-butyric acid	3	50	Water	153–5[e]
DL-α-Amino-*n*-butyric acid	4	54	Benzene	157–8[f]
α-Aminoisobutyric acid	3	60	95%Ethanol	203–5[g]
α-Aminoisobutyric acid	4	59	75% Ethanol	187–9
γ-Amino-*n*-butyric acid	3	82	95% Ethanol	132–3[h]
γ-Amino-*n*-butyric acid	4	40	95% Ethanol	165–6[i]
DL-Norvaline	3	70	3 to 1 C_6H_6–C_6H_{14}	140–2
DL-Norvaline	4	82	Benzene	104–6
DL-Valine	3	84	1 to 2 $CHCl_3$–CCl_4	130–2
DL-Valine	4	82	1 to 2 $CHCl_3$–CCl_4	141–3
DL-Isovaline	3	56	Benzene	159–60.5
DL-Isovaline	4	62	20% Ethanol	153–5
DL-Norleucine	3	59	1 to 1 C_6H_6–C_6H_{14}	113–15
DL-Norleucine	4	82	3 to 1 CCl_4–C_6H_{14}	132–3
DL-Leucine	3	80	2 to 3 $CHCl_3$–CCl_4	152–3.5
DL-Leucine	4	65	CCl_4	136–7
DL-Isoleucine	3	67	1 to 1 $CHCl_3$–CCl_4	160–2
DL-Isoleucine	4	60	1 to 1 C_6H_6–C_6H_{14}	118–19.5
DL-α-Amino-*n*-caprylic acid	3	96	1 to 2 C_6H_6–C_6H_{14}	94.5–5.5
DL-α-Amino-*n*-caprylic acid	4	50	1 to 3 CCl_4–C_6H_{14}	115–16.5
DL-α-Phenylglycine	4	19	Benzene	186–7
DL-Phenylalanine	3	62	1 to 3 Acetone–C_6H_6	203–5
DL-Phenylalanine	4	96	Benzene	208.5–10
1-Amino-1-cyclopentanecarboxylic acid	3	56[j]	Benzene	189–91
1-Amino-1-cyclopentanecarboxylic acid	4	62[j]	2 to 1 EtOH–C_6H_6	158.5–60
DL-Methionine[k]	3	64	2 to 1 C_6H_6–C_6H_{14}	114–16
DL-Methionine[l]	4	77	1 to 1 $CHCl_3$–CCl_4	138–9
DL-Aspartic acid	3	30	Water	230–1
DL-Aspartic acid	4	62	Water	204–5
DL-Glutamic acid[m]	3	13[n]	Water	190–2
DL-Glutamic acid[m]	4	31	Water	227–8

[a] Analysis done by Midwest Microlab, Inc., Indianapolis, Ind., and deposited with ADI. [b] Electrothermal apparatus. [c] Reported (*4*) m.p. 145–8° C. [d] Reported (*4*) m.p. 207–9° C. [e] Reported (*1*) m.p. 154–5° C. [f] Reported (*1*) m.p. 163–4° C. [g] Reported (*4*) m.p. 205–7° C. [h] Reported (*4*) m.p. 134.5–6° C. [i] Reported (*4*) m.p. 165–7° C. [j] Plus 5 to 10% recovery of the amino acid. [k] Anal. Calcd.: S, 9.89; Found: S, 9.84. [l] Anal. Calcd.: S, 9.89; Found: S, 9.85. [m] Although prepared from L(+)-glutamic acid, the derivative was optically inactive. [n] Plus 28% recovery of 3-nitrophthalic acid.

Table II. Aminophthaloyl Derivatives of Amino Acids[a]

Amino Acid	Position of Amino Group	Yield, %	Recrystallized from	M.P., °C.[b]
DL-Alanine	3	85	80% Ethanol	204–5
DL-Alanine	4	80	Water	226–7
β-Alanine	3	90	Water	157–8
β-Alanine	4	68	Water	202–3
DL-α-Amino-*n*-butyric acid	3	75	Benzene	153–4.5
DL-α-Amino-*n*-butyric acid	4	74	75% Ethanol	183–4.5[c]
α-Aminoisobutyric acid	3	72	Water	225–7
α-Aminoisobutyric acid	4	77	50% Ethanol	254–5
γ-Amino-*n*-butyric acid	3	87	Water	160–2
γ-Amino-*n*-butyric acid	4	86	Water	185.5–6.5
DL-Norvaline	3	88	Benzene	156.5–8
DL-Norvaline	4	72	40% Methanol	74–6
DL-Valine	3	60	10% Ethanol	137–8
DL-Valine	4	93	50% Methanol	95–7
DL-Isovaline	3	88	75% Ethanol	199.5–200.5
DL-Isovaline	4	80	50% Ethanol	199–200
DL-Norleucine	4	64	20% Methanol	57–9
DL-Isoleucine	3	92	Benzene	138–40
DL-α-Amino-*n*-caprylic acid	3	77	1 to 1 C_6H_6–C_6H_{14}	113–14.5
DL-α-Amino-*n*-caprylic acid	4	46	1 to 1 $CHCl_3$–CCl_4	142.5–3.5
DL-Phenylalanine	3	68	75% Ethanol	177–8.5
DL-Phenylalanine	4	86	50% Methanol	216–18
1-Amino-1-cyclopentanecarboxylic acid	3	83	Benzene	169.5–70.5
1-Amino-1-cyclopentanecarboxylic acid	4	87	Benzene	223–6
DL-Aspartic acid	3	95	Water	235–7[d]
DL-Aspartic acid	4	81	Water	230–2[d]
DL-Glutamic acid	3	91	Water	214–15
DL-Glutamic acid	4	99	1 to 1 CH_3OH–C_6H_6	205–6

[a] Analysis done by Midwest Microlab, Inc., and deposited with ADI. [b] Electrothermal apparatus. [c] Reported (*1*) m.p. 182–4° C. [d] Decomposition with bubbling.

Aminophthaloyl Derivatives of Amino Acids. Mixtures of 1 to 2 grams of a nitrophthaloyl derivative, 0.3 to 0.5 gram of 10% palladium-charcoal catalyst, and 25 ml. of 95% ethanol were hydrogenated for 1 hour at room temperature in a Parr Model 3910 hydrogenation apparatus, with initial pressures of 65 p.s.i.g. The outgassed mixtures were filtered, and the filtrates were evaporated to dryness on a steam bath. The residues were recrystallized three to five times. The results are summarized in Table II. All of the aminophthalimido acids are bright-yellow, crystalline powders.

ACKNOWLEDGMENT

Thanks are due to Judy Howell for her assistance in the synthesis of some of the nitrophthalimido acids.

LITERATURE CITED

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RECEIVED for review August 10, 1967. Accepted January 11, 1968. Work supported by The Robert A. Welch Foundation through Research Grant No. M-101. Material supplementary to this article has been deposited as Document No. 9822 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington, D. C. 20540. A copy may be secured by citing the document number and by remitting $1.25 for photoprints or $1.25 for 35-mm. microfilm. Advance payment is required. Make checks or money orders payable to Chief, Photoduplication Service, Library of Congress.

CORRECTION

In the article "Metal Complexes of Cyanoformamidines, Oxamidines, and Oxalimidates" by H.M. Woodburn, R.H. Salvesen, J.R. Fisher, W.E. Hoffman, E.L. Graminski, and R.L. VanDeusen [J. CHEM. ENG. DATA **12**, 615 (1967)], the last line in Table II on page 616 should read:

R	*n*	*M*	*x*	Appearance	M.P., °C.
2-Hydroxyethyl	2	Ni	2	Yellow orange powder	224–5 dec.