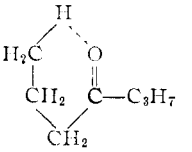
TABLE II

RELATION BETWEEN STRENGTH OF HYDROGEN BOND AND MAGNITUDE OF THE SHIFT

Complex	K	$\Delta\nu$ in cm.$^{-1}$ ± 10 cm.$^{-1}$	Energy in kcal./mole (approximate)
Phenol–acetone	0.118	266	7.0
Phenol–methyl ethyl ketone	.125	230	6.0
Phenol–diethyl ketone	.136	209	5.4
Phenol–4-heptanone	.139	197	5.2
Phenol–acetophenone	.146	243	6.5

Although there is very little difference between the magnitudes of the shifts, the phenol–acetophenone complex does not follow the apparent trend in shifts. Since the equilibrium constant depends upon the entropy as well as the energy, and the shift of the OH frequency is presumed to depend only on the energy of the OH–O bond, the large dissociation constant of the phenol–acetophenone complex may be associated with some type of steric hindrance, possibly between the two large benzene rings. The fact that the OH–O bond for the phenol–acetophenone complex is broader than that of the other complexes further indicates that there may be a steric factor hindering the formation of a definitely oriented complex structure.

According to the theory of the six-membered ketone ring discussed by Newman,[19] it was expected that the 4-heptanone might show intramolecular hydrogen bonding to form the six-membered ring structure



If there were a strong tendency to form this intramolecular bond, one would expect this reaction to compete with the formation of the phenol–4-heptanone complex by intermolecular hydrogen bonding and in this case the dissociation constant of the intermolecular complex should be larger than that for the phenol–diethyl ketone complex. From the results it appears that this intramolecular bond is not sufficiently strong to compete with the phenol, since there is only a small and possibly insignificant increase in K in going from diethyl ketone to 4-heptanone, the values of K being 0.136 and 0.139, respectively.

(19) M. S. Newman, THIS JOURNAL, **72**, 4783 (1950).

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[CONTRIBUTION NO. 2135 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

The Behavior of Several Nitrogenous Compounds in Sulfuric Acid

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It has been shown that the carboxamide group present in glycinamide cation is more basic than the carboxyl group present in glycine cation, that benzoylglycinamide undergoes normal rather than complex ionization in sulfuric acid, that trichloroacetamide, benzenesulfonamide and phthalimide are completely ionized and *o*-benzoicsulfimide is only partially ionized in this solvent, that DL-phenylalanine undergoes rapid nuclear sulfonation under the experimental conditions encountered in cryoscopic studies and that in sulfuric acid benzhydrazide is converted into a mixture of benzoic acid and dibenzhydrazide at temperatures below 25° and into 2,5-diphenyl-1,3,4-oxadiazole at 100°.

Because the simple carboxamides, such as isobutyramide and benzamide, and the corresponding carboxylic acids undergo complete ionization in sulfuric acid[3-6] it is impossible to determine their relative basicities in this solvent. However, it has been reported[7,8] that glycine in sulfuric acid exhibits an *i*-factor of 2.2 and it may be inferred from this observation that the protonation of the carboxyl group of the glycine cation $\overset{+}{N}H_3CH_2CO_2H$ is limited to about 20% of the theoretical amount by the positively charged α-ammonium group present in this molecule. It therefore appeared desirable to compare the cryoscopic behavior of sulfuric acid solutions of glycine and those of glycinamide in order to arrive at an estimate of the relative basicities of the carboxyl and carboxamide groups present in these particular molecules.

In order to bring our observations into proper perspective with those made earlier[6] the cryoscopic behavior of benzamide in sulfuric acid was reinvestigated and an *i*-factor of 2.0 was obtained. This finding is consistent with the earlier conclusion[6] that benzamide is completely ionized as a mono-acid base in sulfuric acid. The cryoscopic properties of sulfuric acid solutions of glycinamide sulfate were then determined and an *i*-factor of 2.7 was obtained. Thus, in contrast to the protonation of the glycine cation $\overset{+}{N}H_3CH_2CO_2H$ which proceeds only to an extent of about 20% in sulfuric acid it is seen that the protonation of the glycinamide cation $\overset{+}{N}H_3CH_2CONH_2$ proceeds to extent of about 70% in the same solvent and that the carboxamide group is more basic than the carboxyl group.

The cryoscopic behavior of benzoylglycinamide in sulfuric acid was then examined and in contrast to benzoylglycine[9,10] the former compound was found to undergo normal rather than complex ionization in sulfuric acid. The observed *i*-factor of

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(2) To whom inquiries regarding this article should be sent.
(3) R. J. Gillespie and J. A. Leisten, *Quart. Revs.*, **8**, 40 (1954).
(4) A. Hantzsch, *Z. physik. Chem.*, **61**, 257 (1907).
(5) G. Oddo and A. Casalino, *Gazz. chim. ital.*, **47**, [2] 200 (1917).
(6) G. Oddo and E. Scandola, *ibid.*, **39**, [1] 569 (1909).
(7) J. L. O'Brien and C. Niemann, THIS JOURNAL, **73**, 4264 (1951).
(8) G. Williams and M. L. Hardy, *J. Chem. Soc.*, 2560 (1953).
(9) J. L. O'Brien and C. Niemann, THIS JOURNAL, **72**, 5348 (1950).
(10) J. L. O'Brien and C. Niemann, *ibid.*, **79**, in press (1957).

2.9 indicates that its ionization as a di-acid base is almost complete in this solvent.

It is of interest to compare the *i*-factor of benzoylglycine ethyl ester, *i.e.*, 2.5,[10] with that of benzoylglycinamide, *i.e.*, 2.9, for these data suggest that the carboxamide group is more basic than the carbethoxy group which in turn has been reported[11] to be more basic than the carboxyl group. The fact that neither benzoylglycine ethyl ester or benzoylglycinamide undergo cyclization in sulfuric acid at 25°, as does benzoylglycine,[9,10] suggests that both the protonated carboxamide group and the protonated carbethoxy group are too weakly electronegative to participate in the required nucleophilic displacement.[9,10]

The above observation on the protonation of the glycinamide cation raised the question as to whether it would be possible to partially repress the protonation of a carboxamide group in sulfuric acid by introducing electronegative but uncharged substituents in the α-position of an amide. The finding that trichloroacetamide in sulfuric acid exhibits an *i*-factor of 2.0 and thus is completely ionized as a mono-acid base in this solvent illustrates the unlikelihood of observing an effect of the above kind and demonstrates that a positively charged α-ammonium group is more effective in repressing the protonation of a carboxamide group by sulfuric acid than are three electronegative chlorine atoms in the α-position.

In a search for other examples of weakly basic nitrogenous compounds the cryoscopic properties of sulfuric acid solutions of benzenesulfonamide, phthalimide and of *o*-benzoicsulfimide (saccharin) were determined. Solutions of both benzenesulfonamide and phthalimide gave *i*-factors very close to 2 and it appears that these two compounds in common with benzamide are practically completely ionized in sulfuric acid and function in this solvent as mono-acid bases. However, the *i*-factor of *o*-benzoicsulfimide was found to be about 1.8 which implies that this latter compound is incompletely ionized in sulfuric acid. It is of interest to note that the *i*-factor of phthalic anhydride, *i.e.*, 1.3,[3] is substantially lower than that of phthalimide, *i.e.*, *ca.* 1.9, and that the basicity of *o*-benzoicsulfimide while possibly less than phthalimide is considerably greater than that of phthalic anhydride.

A cryoscopic examination of the behavior of DL-phenylalanine in sulfuric acid gave an *i*-factor of about 4 and thus indicated that nuclear sulfonation had occurred under the conditions of the cryoscopic measurements. The preparation of *p*-sulfo-DL-phenylalanine by warming the amino acid with a mixture of concentrated and fuming sulfuric acid has been described by Erlenmeyer and Lipp[12] and we have found that the same product is formed when the amino acid is warmed with a limited amount of 100% sulfuric acid. The facile *p*-sulfonation of DL-phenylalanine under the conditions encountered in the cryoscopic measurements is understandable in terms of the explanation given by Gillespie and Leisten[3] although it is surprising to find that the protonated α-amino acid side chain of DL-phenylalanine has such a marked activating effect with respect to nuclear sulfonation.

In the course of our studies need arose for a reference compound which would function as a di-acid base in sulfuric acid and which would be more amenable to manipulation than barium sulfate. It was originally thought that ethylenediamine employed as the crystalline sulfate[13] would satisfy the above requirement and a study of the cryoscopic behavior of ethylenediamine in sulfuric acid was undertaken. While an *i*-factor of approximately 3 was obtained for such solutions it was also noticed that the observed freezing point varied with the age of the solution. An indication of the extent of the dependence of the *i*-factor upon the age of the solution is given by the fact that a 0.0609 molal solution of ethylenediamine sulfate in sulfuric acid giving an initial *i*-factor of 2.86 drifted 0.067° with respect to the freezing point in 24 hours corresponding to an increase of the *i*-factor to 3.04. A control experiment with the solvent alone showed a drift in freezing point of only 0.006° in 25 hours. This slight but definite drift in the freezing point of sulfuric acid solutions of ethylenediamine sulfate suggests that the doubly protonated ethylenediamine reacts slowly with sulfuric acid, possibly to form a sulfamide, and it is clear that the existence of this secondary reaction must be recognized in any study involving the use of ethylenediamine in sulfuric acid solutions.

Having established the extent of ionization of glycine[9,10] and of glycinamide in sulfuric acid we wished to extend our observations to include the corresponding hydrazide. However, a search of the literature failed to disclose any information on the behavior of simple monofunctional hydrazides in sulfuric acid and consequently our attention was first directed to the cryoscopic behavior of a representative monofunctional hydrazide, *i.e.*, benzhydrazide, in sulfuric acid. Although erratic results were obtained in such studies it was clear that benzhydrazide did not undergo normal ionization in sulfuric acid. Therefore, the original goal of this particular study was abandoned and an attempt was made to determine the fate of benzhydrazide in sulfuric acid.

From a solution prepared by adding benzhydrazide to sulfuric acid at 25° there was obtained benzoic acid and dibenzhydrazide. It is known that dibenzhydrazide may be obtained from benzhydrazide by heating the latter compound to 180°,[14] by the oxidation of benzhydrazide with mercuric oxide or with iodine,[15] *via* a base-catalyzed oxidation of the hydrazide[16] or by a base-catalyzed thermal decomposition of the corresponding *sym*-arylsulfonylacyl hydrazide.[17] As in our experiments there was no evidence of the evolution of nitrogen or of sulfur dioxide we are led to believe that dibenzhydrazide arises from benzhydrazide *via* a sulfuric acid-catalyzed elimination reaction possibly of the type

(11) R. A. Craig, A. B. Garrett and M. S. Newman, THIS JOURNAL, **72**, 163 (1950).

(12) E. Erlenmeyer and A. Lipp, *Ann.*, **219**, 209 (1883).

(13) W. Traube and M. Wolff, *Ber.*, **53**, 1501 (1920).

(14) T. Curtius, *J. prakt. Chem.*, II, **50**, 281 (1894).

(15) R. Stollé, *ibid.*, **66**, 338 (1902).

(16) L. Kalb and O. Gross, *Ber.*, **59**, 727 (1926).

(17) C. Niemann and J. T. Hays, THIS JOURNAL, **65**, 482 (1943).

$$2C_6H_5CONHNH_2 + 2H_2SO_4 \longrightarrow {}^{+}{}_{+} C_6H_5CONHNHCOC_6H_5 + H_3NNH_3 + 2HSO_4^-$$

and that the diacylhydrazide so formed may undergo further protonation in sulfuric acid, which species and that arising from the protonation of benzhydrazide may be hydrolyzed during the course of isolation. The fact that only benzoic acid and no benzhydrazide could be obtained from a solution of benzhydrazide in 96% sulfuric acid either at 25 or 100° is consistent with the idea that benzhydrazide in contrast to benzamide[18] is rapidly hydrolyzed in the 96% acid.

In an attempt to increase the yield of dibenzhydrazide by the reaction of benzhydrazide with 100% sulfuric acid the temperature was increased from 25 to 100°. However, in this instance the two products isolated were benzoic acid and 2,5-diphenyl-1,3,4-oxadiazole. The fact that 2,5-diphenyl-1,-3,4-oxadiazole was obtained at 100° is strong presumptive evidence for the formation of dibenzhydrazide as an intermediate and the substantial yield of 2,5-diphenyl-1,3,4-oxadiazole obtained at 100° is understandable when it is realized that this latter compound is much more resistant to hydrolysis than is benzhydrazide or dibenzhydrazide. 2,5-Diphenyl-1,3,4-oxadiazole has been prepared previously by heating dibenzhydrazide in a vacuum at 240°,[19] by heating the diacylhydrazide with phosphorus pentoxide,[20] or by the reaction of hydrazine sulfate with benzoyl chloride.[19] The procedure described in this communication appears to be more attractive from a preparative point of view than any of the above.

In an earlier communication[7] it was noted that the *i*-factors of *o*-, *m*- and *p*-aminobenzoic acid in sulfuric acid are 2.3, 2.7 and 2.8, respectively. From the discussion given previously[7] it is clear that in all of the above cases the amino group is first protonated and that the extent of subsequent protonation of the carboxyl group is largely determined by the position of the carboxyl group relative to the positive charge which is localized in the immediate vicinity of the ammonium group present in the mono-cation. In 1917, Oddo and Casalino[5] reported that terephthalic acid exhibits an *i*-factor of 2.2 in sulfuric acid which implies that in this case monoprotonation of terephthalic acid results in a cation in which the positive charge is not localized in the vicinity of the protonated carboxyl group but instead is distributed over the benzenoid nucleus with the result that the extent of protonation of the remaining *p*-carboxyl group is comparable in magnitude to that observed when an ammonium group with its localized positive charge is *ortho* to a carboxyl group and is very much less than that observed when a positively charged ammonium group is *para* to a carboxyl group. While the above interpretation leads to a reasonable conclusion it was judged worthwhile to reinvestigate the cryoscopic behavior of terephthalic acid in sulfuric acid in order to be certain that the value of Oddo and Casalino,[5] which was determined about forty years ago, was correct. The results of such a study were in excellent agreement with those reported previously.[5]

(18) T. W. J. Taylor and W. Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, 1937, pp. 139, 145.

(19) R. Stollé, *J. prakt. Chem.*, II, **69**, 145 (1904).

(20) R. Stollé and W. Kind, *ibid.*, II, **70**, 423 (1904).

Experimental[21,22]

Cryoscopic Studies.—The apparatus and technique have been described previously.[7,10] The cryoscopic data are summarized in Table I where T is the initial freezing point of the sulfuric acid, Δm the increment in molality of the solution, ΔT the corrected resultant freezing point depression, and i the van't Hoff factor calculated from the relation $i = \Delta T/\Delta m \times 6.154\ (i - 0.0047t)$ where t is the mean depression. It will be noted that in this study as before[7,10] a value of 6.154 was taken as the cryoscopic constant of sulfuric acid. From the data given in Table I it is seen that the *i*-factors of solutions of benzamide, glycinamide, benzoylglycinamide, trichloroacetamide, benzenesulfonamide and phthalimide generally increase with increasing concentration of the solute,[7] that those of *o*-benzoicsulfimide are essentially independent of the concentration of the solute and that those of terephthalic acid decrease with increasing concentration of the solute. All of the solutes except those described below were prepared or purified by standard procedures and whenever possible were dried at 100° and in every case were stored *in vacuo* over sulfuric acid prior to use. Except where noted the *i*-factors were independent of the age of the solution.

TABLE I

PRIMARY CRYOSCOPIC DATA

T, °C.	Δm	ΔT, °C.	i
Benzamide			
10.0	0.0469	0.558	1.94
	.0450	.532	2.01
	.0454	.608	2.20
		Av.	2.0[c]
Glycinamide			
9.2	0.0358	0.595	2.72
	.0351	.573	2.69
	.0357	.660	2.90
10.2	.0313	.493	2.56
	.0362	.592	2.67
	.0462	.812	2.88
		Av.	2.7[c]
Trichloroacetamide			
10.0	0.0298	0.342	1.87
	.0448	.535	1.94
	.0474	.600	2.07
		Av.	2.0[c]
Benzoylglycinamide			
9.9	0.0328	0.556	2.77
	.0329	.583	2.90
	.0363	.695	3.15
		Av.	2.9[c]
Benzenesulfonamide			
9.6	0.0443	0.538	1.98
	.0459	.571	2.04
	.0521	.670	2.11
		Av.	2.0[c]
Phthalimide			
9.7	0.0426	0.483	1.85
	.0539	.624	1.90
	.0359	.436	1.99
		Av.	1.9[c]
o-Benzoicsulfimide			
9.9	0.0533	0.590	1.81
	.0532	.596	1.83
	.0379	.427	1.85
		Av.	1.8[c]
DL-Phenylalanine			
9.9	0.0342	0.806	3.84
	.0528	1.316	4.09
		Av.	4.0[c]
Ethylenediamine			
9.9	0.0154	0.254	2.69
	.0284	.504	2.90
	.0189	.346	3.00
10.2	.0236	.406	2.80
	.0237	.422	2.90
	.0333	.624	3.07
	.0517	1.016	3.23
9.9	.0609	1.066[a]	2.86[a]
	.0609	1.133[b]	3.04[b]
		Av.	2.9[c,d]
Benzhydrazide			
10.0	0.0252	0.439	2.84
	.0283	0.608	3.51
	.0387	1.038	4.10
		Av.	>3.0[c]
Terephthalic acid			
10.1	0.0221	0.306	2.25
	.0357	.475	2.17
	.0405	.528	2.13
		Av.	2.2[c]

[a] Initial value. [b] Value after 24 hours. [c] Differences in averages of 0.1 unit are of questionable significance. [d] Value slowly increases with time, *cf.*, text.

Glycinamide Sulfate.—Eight grams of glycinamide, m.p. 61–63°,[23] was slowly added to a cooled solution of 5.5 g. of 96% sulfuric acid in 20 ml. of water. To this solution was then added with vigorous stirring 150 ml. of absolute ethanol, the suspension cooled to 5°, the crystalline precipitate collected, washed with absolute ethanol and dried at 100°

(21) All melting points are corrected.

(22) Microanalyses by Dr. A. Elek.

(23) P. S. Yang and M. M. Rising, THIS JOURNAL, **53**, 3183 (1931).

to give 12.2 g. (90%) of glycinamide sulfate. This product was dissolved in 20 ml. of water and reprecipitated with 150 ml. of ethanol to give 11.9 g. of product after drying at 100°.

Anal. Calcd. for $C_4H_{14}O_6N_4S$ (244): N, 22.8; S, 13.0. Found: N, 22.9; S, 12.6.

Ethylenediamine Sulfate.[13]—A solution of 10 g. of twice-distilled ethylenediamine in 50 ml. of water was added with stirring to a cooled solution of 17 g. of 96% sulfuric acid in 125 ml. of water. To the resultant solution was added 150 ml. of ethanol, the crystalline precipitate collected, washed with absolute ethanol and air-dried to give 24.2 g. (90%) of the desired product which was reprecipitated from an aqueous solution by the addition of an equal volume of ethanol.

Anal. Calcd. for $C_2H_{10}O_4N_2S$ (158): C, 15.2; H, 6.4; N, 17.7; S, 20.3. Found: C, 15.5; H, 6.7; N, 17.4; S, 20.4.

***p*-Sulfo-DL-phenylalanine.**[12]—The reaction of 33 g. of DL-phenylalanine and 50 ml. of 100% sulfuric acid essentially as described by Erlenmeyer and Lipp[12] gave 20.8 g. of a white solid and 15 g. of a glassy amber resin. The white solid proved to be *p*-sulfo-DL-phenylalanine monohydrate.[12]

Anal. Calcd. for $C_9H_{13}O_6NS$ (263): C, 41.1; H, 5.0; N, 5.3; S, 12.2. Found: C, 41.1; H, 4.9; N, 5.5; S, 12.1.

Reaction of Benzhydrazide with 96% Sulfuric Acid.—(A) Five grams of benzhydrazide, m.p. 113–114°, was dissolved in 15 ml. of 96% sulfuric acid with the temperature being maintained below 25°. Five minutes after solution was effected the mixture was poured into 50 ml. of ice-water, the precipitate collected, washed with water and dried. The weight of the solid, completely soluble in aqueous sodium bicarbonate, was 1.0 g. This product was benzoic acid, m.p. 121–122°. (B) In a second experiment a solution of benzhydrazide, 5 g., in 15 ml. of 96% sulfuric acid was heated on a steam-bath for 1.5 hours, the solution cooled, poured into 50 ml. of ice-water, the precipitate collected and washed with water. This product was recrystallized from 200 ml. of water to give 3.7 g. of benzoic acid, m.p. 121–122°. (C) The above experiment was repeated using benzamide instead of benzhydrazide. The product isolated was insoluble in aqueous sodium bicarbonate and proved to be benzamide, m.p. 125–126°. The yield was 3.1 g.

Reaction of Benzhydrazide with 100% Sulfuric Acid.—(A) To 15 ml. of a solution of benzhydrazide in 100% sulfuric acid obtained from a freezing point determination (containing 0.35 g. of benzhydrazide) was added an additional 5.0 g. of benzhydrazide maintaining the temperature of the solution below 25°. The solution was allowed to stand at 25° for 30 minutes and then poured into 50 ml. of ice-water. The precipitate was collected and washed with cold water. This precipitate was fractionated into bicarbonate-soluble and bicarbonate-insoluble fractions. The bicarbonate soluble fraction, 1.2 g., proved to be benzoic acid, m.p. 121–122°. The bicarbonate-insoluble fraction, 0.9 g., was recrystallized from 30 ml. of 95% ethanol to give dibenzhydrazide, m.p. 241–242°, lit.[24] 241–242°. (B) To 35 ml. of a solution of benzhydrazide in 100% sulfuric acid employed in a freezing point determination was added sufficient benzhydrazide, *i.e.*, 9.2 g., to bring the total amount to 10.0 g. The solution was heated on a steam-cone for 90 minutes, the clear yellow-orange solution cooled and poured into 150 ml. of ice-water. The copious colorless precipitate was collected, washed with water and then triturated with aqueous sodium bicarbonate. The insoluble fraction was collected and dried at 105° to give 4.8 g. of product. This product was dissolved in 50 ml. of glacial acetic acid, the solution poured into 250 ml. of water, the precipitate collected and dried to give 3.6 g. of product, m.p. 138.5–139.5°. Recrystallization of this product from 95% ethanol gave 2,5-diphenyl-1,3,4-oxadiazole, m.p. 139–140°.

Anal. Calcd. for $C_{14}H_{10}ON_2$ (222): C, 75.7; H, 4.5; N, 12.6. Found: C, 75.7; H, 4.6; N, 12.5.

Stollé[25] gives a m.p. of 138° for the above compound. Acidification of the sodium bicarbonate solution obtained above gave 1.7 g. of benzoic acid, m.p. 121.5–122.5° after recrystallization from water. It will be noted that the yield of 2,5-diphenyl-1,3,4-oxadiazole was 59% based upon the crude product.

(24) R. S. Curtiss, A. R. Koch and E. J. Bartells, THIS JOURNAL, **31**, 420 (1909).

(25) R. Stollé, *J. prakt. Chem.*, II, **69**, 145 (1904).

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[CONTRIBUTION NO. 2141 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Some Reactions of α-Phthalimidonitriles Including Those Leading to the Synthesis of α-Aminoamidoximes and α-Aminothioamides[1]

BY PAUL E. PETERSON AND CARL NIEMANN[2]

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It has been shown that DL- and L-α-phthalimido-β-phenylpropionitrile may be prepared by the dehydration of the corresponding amides. The reaction of DL- and L-α-phthalimido-β-phenylpropionitrile with hydroxylamine has been found to give the corresponding amidoximes which in turn may be transformed, with the aid of hydroxylamine, into the corresponding α-aminoamidoximes. These latter compounds were acylated to give the corresponding O,N-diacetyl- and O,N-dibenzoylamidoximes which were then converted into the corresponding α-acetamido- and α-benzamidoamidoximes by reaction with methanolic sodium methoxide. DL-α-Phthalimido-β-phenylpropionitrile, after preliminary ammonolysis, was shown to react with hydrogen sulfide to give DL-α-phthalamamido-β-phenylthiopropionamide which, with the aid of a new cleavage procedure, was converted into DL-α-amino-β-phenylthiopropionamide. This latter compound was acetylated to give DL-α-acetamido-β-phenylthiopropionamide. DL-α-Phthalimido-β-phenylpropionitrile was observed to react with methanolic hydrogen chloride to give the corresponding imino ester and to be reduced with stannous chloride to give the corresponding aldehyde.

It is well known that esters, hydroxamides, amides and hydrazides of certain α-amino acids or acylated α-amino acids may serve as specific substrates for at least one of the proteolytic enzymes, *i.e.*, α-chymotrypsin. However, in all of the above derivatives the carbonyl group associated with the hydrolyzable bond is a common structural feature and nothing is known of the behavior of those derivatives in which the oxygen atom of this carbonyl group is replaced by another atom or group. Therefore, in order to investigate the consequences of such a structural change in a molecule otherwise capable of functioning as a specific substrate for α-chymotrypsin, we have directed our attention to the development of synthetic procedures for the preparation of α-amino acid derivatives in which the carbonyl oxygen atom associated with the potential carboxyl group of the α-amino acid is replaced by another atom or group. In this com-

(1) Supported in part by a grant from the National Institutes of Health, Public Health Service.

(2) To whom inquiries regarding this article should be sent.