p-aminobenzamidomalonic acid, modified as for II above (see Table III). Also, V was synthesized by a variation of the procedure employed by Hultquist and Dreisbach using 1,1,3-tribromoacetone.[9] The crude product prepared by the latter method contained about 30% of the desired compound, as estimated by the chemical assay of Hutchings, *et al.*[14] The crude was dissolved in 5% sodium carbonate solution at a concentration of 6 g. of V per liter, filtered, and the filtrate was acidified to *p*H 4 and cooled several hours at 2°. The precipitate was collected on the filter and washed with ice water, and then crystallized (at 5 g./l.) three times from hot 0.1 *N* hydrochloric acid. The material thus obtained had a chemical assay[14] of 66.4%.

4-Aminopteroylserine (VI).—This compound was synthesized from N-(*p*-aminobenzoyl)-serine by the method of Waller, *et al.*,[7] as modified for II above (see Table III) and also by a variation of the procedure of Hultquist and Dreisbach,[9] as indicated above for V. The crude material was heated at 60° with lime in water at a concentration of VI of 1 g./l. The solution was filtered and the filtrate was adjusted to *p*H 10.5–11.0 with aqueous zinc chloride. Insolubles were removed by filtration and the solution was acidified to *p*H 4, and the precipitated material was collected on the filter. It was extracted with 0.1 *N* hydrochloric acid at 80°. The residue was dissolved in dilute sodium hydroxide and reprecipitated with acid at 80°; after cooling to 10° the yellow, partially crystalline product obtained was filtered and dried. It showed a chemical assay[14] of about 70%. It was purified further by repeating the process above and then extracting with 0.1 *N* hydrochloric acid and reprecipitating three times more.

Anal. Calcd. for $C_{17}H_{18}O_4N_8{\cdot}3H_2O$: C, 45.1; H, 5.35; N, 24.7; H_2O, 11.9. Found: C, 45.3; H, 5.15; N, 24.7; H_2O, 9.9.

The hot 0.1 *N* hydrochloric acid extracts contain additional 4-aminopteroylserine which can be recovered by cooling and reworking as above.

Other Pteroyl- and 4-Aminopteroylamino Acids.—These were prepared by the method of Waller[7] from the N-(*p*-aminobenzoyl)-amino acids. One-half an equivalent of iodine or sodium dichromate was added during the condensation.

Acknowledgment.—We are indebted to Mr. Kenneth H. Collins for technical assistance in this investigation, to Miss Ruth Abbott for the ultraviolet absorption spectra studies, and to Mr. O. Sundberg and co-workers for the microanalyses.

Summary

1. The N-(*p*-nitrobenzoyl) derivatives of β-alanine, ε-aminocaproic acid, diethyl aminomalonate, isoleucine, sarcosine and tryptophan, have been prepared.

2. The N-(*p*-aminobenzoyl) derivatives of the following amino acids have been prepared: alanine, β-alanine, ε-aminocaproic acid, aminomalonic acid, isoleucine, phenylalanine, serine, threonine, tryptophan, and valine.

3. Pteroyl derivatives of alanine, ε-aminocaproic acid, aminomalonic acid, isoleucine, phenylalanine, sarcosine, serine, threonine, tryptophan, valine, β-alanine, cystine and methionine have been prepared as crude reaction products. With the exception of the last three, the corresponding 4-aminopteroylamino acids also have been prepared.

4. Pteroylalanine, pteroyl-β-alanine, pteramidomalonic acid, and 4-aminopteroylserine have been purified.

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[Contribution from the Eastern Regional Research Laboratory[1]]

Fatty Acid Amides. II.[2] Amides as Derivatives for the Identification of Some Long-Chain Unsaturated Fatty Acids

By Daniel Swern, Jeanne M. Stutzman and Edward T. Roe

Four techniques are usually employed for the identification of long-chain unsaturated fatty acids. They are (a) rigorous purification of the acid, followed by comparison of its properties with those of the acid with which it is presumed to be identical, (b) cleavage of the acid by any one of several well-known procedures, followed by identification of the fragments, (c) preparation of relatively high melting derivatives involving the ethylenic system, and (d) preparation of derivatives involving the carboxyl group.[3] The relatively high solubility of unsaturated fatty acids in organic solvents, their tendency to form crystalline mixtures of invariant composition, and the need for extremely low temperatures in their isolation and purification render the first technique time-consuming and impractical, and often it does not produce a product of sufficiently high purity, particularly when complex mixtures of fatty acids are employed as the starting material. The second technique is time-consuming, and in addition the severe conditions sometimes required to cleave the chain may cause isomerization. Furthermore, this technique may not give definitive results because of poor yields of cleavage products and the fact that the stereochemical nature of the parent acid cannot be deduced after the molecule is degraded. The third technique, which is the one most widely used, generally involves the formation of brominated or hydroxylated products. Although quantitative

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(2) For the first paper in this series, see This Journal, **71**, 2215 (1949).

(3) Shriner and Fuson, "The Systematic Identification of Organic Compounds," 2nd Edition, John Wiley and Sons, Inc., New York, N. Y., 1940: McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1945; Wild, "Characterization of Organic Compounds," University Press, Cambridge, England, 1947.

TABLE I

CHARACTERISTICS OF AMIDES OF SOME UNSATURATED ACIDS

Number	Acid	Unsubstituted amide M. p., °C.	Iodine no.[a] Calcd.	Iodine no.[a] Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
1	Oleic[b]	76	90.2	90.2	76.8	77.0	12.5	12.4	4.97	4.91
2	Elaidic	90[c]	90.2	90.2	76.8	77.1	12.5	12.7	4.97	4.91
3	Linoleic									
4	Ricinoleic									
5	10-Hendecenoic	87.0–87.5[d]	138.5	135.7[e]	..	..	..	..	7.64	7.53

[a] One-half hour Wijs method. [b] Data taken from the paper by Roe, Scanlan and Swern.[2] [c] Emeljanoff and Albitzky[9] give 93–94°. [d] Jones and Pyman, *J. Chem. Soc.*, **127**, 2588 (1925), give 87°. [e] Micro-hydrogenation no. 8: Calcd. 183.3; found 183.9.

TABLE II

CHARACTERISTICS OF N-SUBSTITUTED AMIDES OF SOME UNSATURATED ACIDS

No. from Table I	N-(2-Hydroxyethyl)-amide M. p., °C.	Iodine No.[a] Calcd.	Iodine No.[a] Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	N(*n*-Dodecyl)-amide M. p., °C.	Iodine No.[a] Calcd.	Iodine No.[a] Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
1	63–64[b]	78.0	78.0	73.8	74.4	12.1	12.1	4.31	4.38	53.5–54.0	56.4	56.1	80.1	79.8	13.2	12.9	3.11	3.07
2	87	78.0	78.1	73.8	73.7	12.1	12.2	4.31	4.19	75.0–75.5[c]	56.4	56.2	80.1	80.1	13.2	13.3	3.11	3.06
3	39.0–39.5	156.9	157.5	74.3	74.3	11.5	11.3	4.33	4.13	45.5–46.0	113.4	114.2	80.5	80.6	12.8	12.9	3.13	3.00
4	54.5–55.0	74.3	74.8	70.3	70.4	11.5	11.7	4.10	4.25	56.0–57.0	54.5	54.3	77.4	77.2	12.8	13.0	3.01	2.90
5	67.0–67.5[d]	111.7	111.4	68.7	68.5	11.1	11.5	6.16	6.05	61.5–62.5	72.2	69.6[e]	78.6	78.3	12.9	12.8	3.98	4.02

[a] One-half hour Wijs method. [b] Hydroxyl: calcd., 5.22; found, 5.18. [c] Harber, *Iowa State Coll. J. Sci.*, **15**, 13 (1940), gives 73.5–74.0°. [d] Széki, *Math. naturw. Aus. ungar. Akad. Wiss.*, **54**, 807 (1936), gives 70.5°. [e] Micro-hydrogenation No. 8: Calcd., 351.6; found, 356.4.

hydroxylation of mono-unsaturated acids is conveniently carried out,[4] and this technique has some promise for identification purposes, the impossibility of regenerating the parent acid from the derivative by any simple procedure is a disadvantage. Furthermore, poly-unsaturated acids cannot be hydroxylated in good yields by any of the methods known at present, and the products obtained consist of mixtures of isomers difficult or impossible to separate. Poly-unsaturated acids are usually identified as polybromo acids, and the disadvantages of this technique have already been pointed out.[5] The fourth technique, however, appears to have none of the drawbacks of the others. This technique has been explored somewhat,[5,6,7] but the emphasis has been primarily on the preparation of esters, which not only have relatively low melting points, but in esters of poly-unsaturated acids do not give the calculated analytical values.

Amides are among the highest melting fatty acid derivatives, and although considerable reliable data are available on the long-chain saturated acids, the literature on amides of unsaturated fatty acids is generally incomplete and often unreliable. This paper describes the preparation and some of the properties of the unsubstituted, the N-(2-hydroxyethyl)-, and the N-(*n*-dodecyl)-amides of linoleic, ricinoleic, 10-hendecenoic (undecylenic) and elaidic acids. The results are summarized in Tables I and II (the characteristics of the corresponding amides of oleic acid, taken from a previous paper,[2] are included for comparison).

The unsubstituted amides of oleic,[2] 10-hendecenoic and elaidic acids, and the N-(2-hydroxyethyl)- and N-(*n*-dodecyl) amides of oleic, linoleic, ricinoleic, 10-hendecenoic and elaidic acids were readily prepared in good yield. They were white, crystalline solids which had the calculated analytical characteristics. N-(2-Hydroxyethyl)-hendecenamide had a strong pepper-like taste. We were unable to purify linoleamide, and this amide, as well as N-(2-hydroxyethyl)-linoleamide, rapidly became rancid and dark at room temperature. They were soon converted to viscous, brown oils, although all operations on these and the other amides described were conducted in an atmosphere of nitrogen, and the samples were stored under nitrogen. These two amides undoubtedly undergo rapid oxidation and polymerization in the presence of small quantities of oxygen. N-(*n*-Dodecyl)-linoleamide, however, was much more stable than the other linoleamides, and after storage for several months it was only pale yellow and slightly rancid. The amides of the monounsaturated acids were stable, provided that they were not heated in air. It was essential to dry the amides in an atmosphere of nitrogen, otherwise incorrect analytical values were obtained. Some difficulty was experienced in obtaining theoretical iodine values on purified 10-

[4] Swern, Billen, Findley and Scanlan, THIS JOURNAL, **67**, 1786 (1945).

[5] Kass, Nichols and Burr, *ibid.*, **64**, 1061 (1942).

[6] Drake and Bronitsky, *ibid.*, **52**, 3715 (1930).

[7] Kimura, *J. Soc. Chem. Ind. Japan*, **37**, 154B (1934).

hendecenamide and N-(*n*-dodecyl)-hendecenamide, even though the elemental analyses were correct. The iodine values obtained on these two compounds were usually about two to three units lower than the calculated values, but microhydrogenation numbers were satisfactory.[8] It has been reported that elaidamide melts at 93–94°,[9] but the highest melting point we were able to obtain was 90°, even though we worked with carefully purified materials. The melting points of oleamide (76°) and elaidamide (90°) differ significantly and are readily duplicated, even though widely different preparative reactions are employed. This is good evidence that the conventional reactions for preparing amides[2] do not cause *cis–trans* isomerization.

In the hydrolysis of N-(*n*-dodecyl)-amides to the acid and amine hydrochloride by refluxing with constant boiling hydrochloric acid, approximately twelve hours reflux time was required, and acid fractions with iodine numbers only about one-third or one-fourth those calculated were obtained. The hydrolysis of the unsubstituted or 2-hydroxyethyl amides, however, was complete in about one hour when a large excess (about 500%) of constant boiling hydrochloric acid was employed, and the iodine numbers of the acid fractions were over 90% of those calculated.

In view of the low melting points and relative instability of the linoleamides, no attempt was made to prepare the corresponding amides of linolenic and eleostearic acids, since these would be expected to have even lower melting points and to be less stable.

Experimental[9a]

Materials Used.—Linoleic acid, iodine number 180.3, was prepared by the debromination of 9,10,12,13-tetrabromostearic acid, m. p. 115.0–115.3°, with zinc dust in diethyl ether solution.[10] Methyl ricinoleate, b. p. 196–199° (2.3–2.5 mm.), n^{30}_{D} 1.4598, iodine number 81.3, was prepared from castor oil by methanolysis, followed by fractional distillation through a Vigreux column 3 feet long and 1 inch in diameter.[11] 10-Hendecenoic acid, m. p. 24.3–24.5°, b. p. 180° (26.5 mm.), iodine number 137.2, was prepared[12] from the purest commercial grade by fractional distillation, and crystallization from petroleum naphtha, hexane fraction, at −20°. Elaidic acid, m. p. 44°, was prepared from oleic acid by isomerization with powdered selenium.[13] Monoethanolamine and dodecylamine were the purest commercial grades, and they were distilled before use through efficient fractionating columns.

Preparation of Derivatives. Unsubstituted Amides.—Linoleic, 10-hendecenoic and elaidic acids were converted to the corresponding acid chlorides by reaction with oxalyl chloride in benzene solution, as described by Bauer.[14] After removal of benzene and excess oxalyl chloride, the acid chlorides were added dropwise to a large excess (500–900%) of ice-cold concentrated aqueous ammonium hydroxide, with stirring. The crude amides were separated from the aqueous layer and dissolved in a suitable solvent (petroleum naphtha was employed for linoleamide, and 95% ethanol was employed for 10-hendecenamide and elaidamide; 4 to 5 ml. of solvent per gram of solute), treated with activated carbon and filtered. The filtrates were cooled to 0 to 5° (room temperature in the case of elaidamide), and the amides which precipitated were filtered off and washed with cold solvent. Linoleamide was obtained as a white solid which could not be completely purified. Additional manipulation caused both the melting point and iodine number to decrease. On standing, the product, which contained 0.44% of chlorine, rapidly darkened and became rancid, and it was soon converted to a brown viscous oil. 10-Hendecenamide and elaidamide were white crystalline solids, which were purified by recrystallization from 95% ethanol at 15 to 25°. They were stable at room temperature. Since ricinoleic acid is difficult to purify and is reported to be unstable, no attempt was made to prepare ricinoleamide from it.

N-(2-Hydroxyethyl)-amides.—Linoleic, 10-hendecenoic and elaidic acids, and methyl ricinoleate were refluxed with a 50% molar excess of monoethanolamine (methyl ricinoleate, one hour reflux; the others, two hours). The cooled reaction mixtures were dissolved in petroleum naphtha, 95% ethanol, petroleum naphtha and acetone, respectively (3 to 8 ml. of solvent per gram of solute). The solutions were treated with activated carbon and filtered. The filtrates were cooled (N-(2-hydroxyethyl)-elaidamide, 25°; N-(2-hydroxyethyl)-linoleamide, 0°; the others, −20°) to precipitate the amides, which were filtered off and washed with cold solvent. The products were then recrystallized to constant melting point (N-(2-hydroxyethyl)-elaidamide from 95% ethanol at 10°). N-(2-Hydroxyethyl)-linoleamide was unstable.

N-(*n*-Dodecyl)-amides.—Linoleic, 10-hendecenoic and elaidic acids, and methyl ricinoleate were heated at 230° with a 1% molar excess of *n*-dodecylamine (methyl ricinoleate, three-hour reaction period; the others, thirty-five minutes). The cooled reaction mixtures were dissolved in 95% ethanol (4 to 5 ml. of solvent per gram of solute), the solutions were treated with activated carbon and filtered. The filtrates were cooled to 0° (N-(*n*-dodecyl)-elaidamide was crystallized at 25°), and the precipitated amides were filtered off and washed with cold solvent. The products were then recrystallized to constant melting points.

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Summary

N-(2-Hydroxyethyl)- and N-(*n*-dodecyl)-linoleamides, ricinoleamides, elaidamides and 10-hendecenamides, as well as the unsubstituted amides, elaidamide and 10-hendecenamide, have been prepared and characterized. These amides are suitable derivatives for the identification of the parent unsaturated acids. Linoleamide could not be completely purified. This compound, as well as N-(2-hydroxyethyl)-linoleamide, was unstable at room temperature, both being rapidly converted to dark-brown viscous oils.

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(8) Ogg and Cooper, paper presented at the meeting-in-miniature of the Philadelphia Section of the American Chemical Society, January 20, 1949.

(9) Emeljanoff and Albitzky, *J. Russ. Phys.-Chem. Soc.*, **31**, 106 (1899).

(9a) All operations were conducted in an atmosphere of nitrogen.

(10) Frankel and Brown, THIS JOURNAL, **65**, 415 (1943).

(11) Kass and Radlove, *ibid.*, **64**, 2253 (1942).

(12) Jordan and Swern, *ibid.*, **71**, 2377 (1949)

(13) Bertram, *Chem. Weekblad*, **33**, 3 (1936)

14) Bauer. *Oil and Soap*, **23**, 1 (1946)