organic layer was separated, washed with 2 N hydrochloric acid and with water and filtered with charcoal. The solution was then dried over Drierite and the solvent removed under reduced pressure. The resulting oil, 21 g. (41%), was crystallized from Skellysolve C to furnish a product that melted at 100.9–103.0° (cor.).

Anal. Calcd. for $C_{13}H_9Cl_8NO_3$: C, 30.56; H, 1.78; Cl, 41.65. Found: C, 30.45; H, 1.68; Cl, 41.44.

In a previous run about 10% of 3-(2,4-dichlorobenzyl)-2-oxazolidone[3] was obtained by concentration of the Skellysolve C filtrate. About 30% of unreacted N-(2-hydroxyethyl)-2,4-dichlorobenzylamine also was recovered from the acid washings.

N-(2-Dichloroacetoxyethyl)-2,4-dichlorobenzylamine Hydrochloride.—Anhydrous hydrogen chloride was bubbled into a mixture of 16.6 g. (0.05 mole) of N-(2,4-dichlorobenzyl)-N-(2-hydroxyethyl)-dichloroacetamide and 50 ml. of anhydrous dioxane. The temperature rose to 70° and a clear solution was obtained. The solution was cooled and the solid that separated was collected on a filter and washed with ether, 16 g. (86%). When recrystallized from isopropyl alcohol the hydrochloride salt melted at 146.2–147.1° (cor.).

Anal. Calcd. for $C_{11}H_{11}Cl_4NO_2 \cdot HCl$: C, 35.94; H, 3.29; Cl^-, 9.65. Found: C, 36.35; H, 3.35; Cl^-, 9.63.

N-(2-Dichloroacetoxyethyl)-N-(2,4-dichlorobenzyl)-trichloroacetamide.—A mixture of 13 g. (0.035 mole) of N-(2-dichloroacetoxyethyl)-2,4-dichlorobenzylamine hydrochloride and 9.1 g. (0.05 mole) of trichloroacetyl chloride in 50 ml. of dry benzene was refluxed until a complete solution was obtained. This required about 1.5 hours. Ten milliliters of ethanol was added slowly and the solvent then distilled under reduced pressure. The resulting oily product solidified on treatment with isopropyl alcohol, 15 g. (87%), and after recrystallization from isopropyl alcohol melted at 72.9–76.8° (cor.).

Anal. Calcd. for $C_{13}H_{10}Cl_7NO_3$: C, 32.79; H, 2.11; Cl, 52.11. Found: C, 32.96; H, 2.08; Cl, 51.80.

N-(2,4-Dichlorobenzyl)-N-(2-diethylaminoacetoxyethyl)-dichloroacetamide.—To a refluxing solution of 13.5 g. (0.039 mole) of N-(2-chloroacetoxyethyl)-N-(2,4-dichlorobenzyl)-dichloroacetamide in 75 ml. of benzene was added dropwise 15.7 g. (0.078 mole) of diethylamine. Refluxing was continued for 5 hr. The solid diethylamine hydrochloride was filtered off and the benzene solution washed with water, dried and the solvent removed under reduced pressure. The resulting oily product solidified, 8 g. (55%), which after recrystallization from Skellysolve B melted at 61.1–63.5° (cor.).

RENSSELAER, N. Y.

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

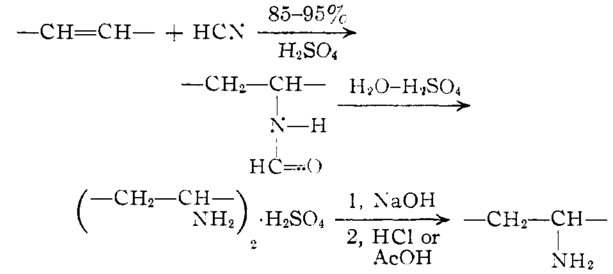
Fatty Acid Amides. VII.[2] Addition of Hydrogen Cyanide to Unsaturated Acids. Preparation of Formamido Acids, Amino Acid Sulfates and Amino Acids

BY EDWARD T. ROE AND DANIEL SWERN

RECEIVED MAY 26, 1955

Liquid hydrogen cyanide has been added to the double bonds of oleic, 10-hendecenoic and ricinoleic acid in 85–95% sulfuric acid to give good yields of formamidostearic, formamidohendecanoic and hydroxyformamidostearic acids, respectively. The first two are rapidly hydrolyzed by refluxing with aqueous sulfuric acid to give the corresponding amino acid sulfates in high yield. These can be converted to the free amino acids by neutralization.

In our previous publication,[2] we reported the addition of various nitriles to the double bond of oleic acid in concentrated sulfuric acid to give substituted amidostearic acids. With the object of preparing more readily hydrolyzable amido acids, we have studied the similar addition of hydrogen cyanide to oleic, 10-hendecenoic and ricinoleic acids to yield formamidostearic, formamidohendecanoic and 12-hydroxyformamidostearic acids, respectively. The general equations show the reactions involved. As anticipated,[2] mixtures of isomeric products are obtained.



$$—CH{=}CH— + HCN \xrightarrow[H_2SO_4]{85\text{–}95\%} \underset{\underset{HC=O}{|}}{\underset{N—H}{|}}{—CH_2—CH—} \xrightarrow{H_2O\text{–}H_2SO_4}$$

$$\left(\begin{array}{r}—CH_2—CH—\\ NH_2\end{array}\right)_2 \cdot H_2SO_4 \xrightarrow[2,\ HCl\ or\ AcOH]{1,\ NaOH} \underset{NH_2}{\underset{|}{—CH_2—CH—}}$$

Hydrogen cyanide in sulfuric acid has been added to the double bonds of reactive olefins, such as diisobutylene,[3] camphene,[3] bimethallyl[4] and limonene,[4] but no work appears to have been published on such reactions with relatively unreactive double bonds.

Experimental

Starting Materials.—Pure oleic acid was obtained from olive oil fatty acids.[5] Ricinoleic acid was prepared from pure methyl ricinoleate[6] by conventional means. 10-Hendecenoic acid was obtained from the purest commercial grade.[7] Anhydrous hydrogen cyanide was prepared as needed from sodium cyanide and sulfuric acid.[8] *All reactions with hydrogen cyanide were conducted in an efficient hood.*

Formamidostearic Acids.—Simultaneously and with efficient stirring, 99 g. (0.35 mole) of oleic acid and 82 ml. (2.1 mole) of liquid hydrogen cyanide contained in a specially constructed jacketed dropping pipet (jacket filled with chopped ice) were added in one-half hour to 318 ml. (4.9 moles) of 85% sulfuric acid in a 2-l. three-neck flask. The reaction was exothermic. The temperature was maintained between 20–30° by controlling the rate of addition of the reactants and by external cooling. Stirring was continued for an additional 1.5 hours and the reaction mixture was poured with stirring onto about 3 l. of chopped ice and water. The mixture was allowed to stand for about two hours with occasional stirring, and the aqueous layer was decanted and

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(1) A laboratory of the Eastern Utilization Research Branch, Agricultural Research Service, United States Department of Agriculture. Article not copyrighted.

(2) For paper VI, see THIS JOURNAL, **75**, 5479 (1953).

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discarded. The amber oil was washed once with cold water to remove unreacted hydrogen cyanide.

For analysis, a small portion of the reaction product was dissolved in ether and the ether solution was washed with water until free of acid. The ether solution was dried over anhydrous sodium sulfate, filtered and the ether was evaporated. (In runs smaller than the one described above, the entire reaction product was worked up in this way; yields were 96–97%.)

Anal. Calcd. for formamidostearic acids, $C_{19}H_{37}NO_3$: N, 4.28; S, 0; acid number, 171; sapn. number, 171; iodine number, 0. Found: N, 3.4; S, 0; acid number, 166; sapn. number, 171; iodine number, 1.5. (In other preparations, N ranged from 3.3–3.9.)

Two crystallizations from ether at −30° (4 ml. of solvent per g. of solute and 10 ml./g.) gave a 21% over-all yield of analytically pure formamidostearic acids, m.p. 42–43°.

Anal. Calcd.: C, 69.7; H, 11.4; N, 4.28. Found: C, 69.9; H, 11.3; N, 4.14.

Aminostearic Acid Sulfates.—Crude formamidostearic acids (100 g.) were refluxed with 400 ml. of 50% aqueous sulfuric acid with simultaneous removal of formic acid by steam distillation. Aliquots of the steam distillate were titrated with 0.1 *N* sodium hydroxide. After five hours hydrolysis was at least 96% complete. The non-volatile product was washed with hot water by decantation until the washes were free of sulfuric acid. It was a brown solid.

One crystallization from 95% ethanol at 0° (6 ml. of solvent per g. of solute) yielded 76 g. (67%) of moderately pure aminostearic acid sulfates. After two additional crystallizations, with carbon treatments, the analytically pure product, m.p. 112.5–132°, was obtained in 40% over-all yield as a white crystalline solid.

Anal. Calcd. for $C_{36}H_{76}N_2O_8S$: C, 62.0; H, 11.0; N, 4.02; S, 4.60. Found: C, 61.8; H, 11.0; N, 4.00; S, 4.52.

Aminostearic Acids.—Crude aminostearic acid sulfates were dissolved in a sufficient excess of aqueous sodium hydroxide to bring the *p*H of the solution to 12. Dilute hydrochloric acid was added with stirring[2] to reduce the *p*H to 5–6, or acetic acid was added until the *p*H was 6.5–7.0. The oil which separated was caused to solidify in the refrigerator and the aqueous layer was discarded. The solid was washed twice by melting with hot water followed by resolidification. The yield of crude aminostearic acids obtained from the sulfates was nearly quantitative.

Anal. Calcd.: neut. equiv., 299; Cl, 0; ash, 0. Found: neut. equiv., 304 (formaldehyde present); Cl, 0.40 (when HCl was used for neutralization); ash, 0.57 (when acetic acid was used for neutralization).

Formamidohendecanoic Acids.—These were prepared as described under formamidostearic acid from 55 g. (0.3 mole) of 10-hendecenoic acid, 35 ml. (0.9 mole) of hydrogen cyanide and 117 ml. (1.8 moles) of 85% sulfuric acid. The yield of crude formamidohendecanoic acids, a dark amber liquid, was 55 g. (80%).

Anal. Calcd. for $C_{12}H_{23}NO_3$: N, 6.11; S, 0; acid number, 245; sapn. number, 245; iodine number, 0. Found: N, 5.60; S, 0; acid number, 237; sapn. number, 252; iodine number, 1.5 (in other runs, N varied from 5.5–5.9).

Three crystallizations from acetone and one from 95% ethanol yielded only 16% of a solid, m.p. 91–93°, the analysis of which was not quite within the acceptable limits for pure formamidohendecanoic acid.

Acid. Calcd.: C, 62.9; H, 10.1; N, 6.11; acid number, 245. Found: C, 64.3; H, 10.6; N, 5.85; acid number, 237.

Aminohendecanoic Acid Sulfates.—These were prepared by hydrolysis of 25 g. (0.1 mole based on N analysis) of crude formamidohendecanoic acid with 100 ml. of 10% sulfuric acid, as described under aminostearic acid sulfate. Since the hydrolysis product was water soluble, the sulfuric acid was neutralized with the calculated amount of dilute sodium hydroxide and the solution was evaporated to dryness on the steam-bath. The solid residue was broken up and extracted with absolute methanol. The methanol solution was evaporated to dryness and the soft wax-like residue was again extracted with absolute methanol. Evaporation of the methanol solution yielded 24 g. (97%) of crude aminohendecanoic acid sulfates.

Anal. Calcd. for $C_{22}H_{48}N_2O_8S$: C, 52.8; H, 9.66; N, 5.60; S, 6.40; iodine number, 0. Found: C, 54.7; H, 9.96; N, 5.30; S, 5.75; iodine number, 2.

Two crystallizations from 95% ethanol (5 and 12 ml./g.) at −25° and −16°, respectively, with carbon treatments, gave the analytically pure product as a white crystalline solid, m.p. 176–177°, in 58% yield.

Anal. Found: C, 52.8; H, 9.67; N, 5.32; S, 6.03.

Aminohendecanoic Acids.—Aqueous 1 *N* sodium hydroxide was added to 7.6 g. of pure aminohendecanoic acid sulfates to *p*H 12. Excess 90% acetic acid was added and the solution was evaporated to dryness. The solid residue was crystallized from 50 ml. of absolute methanol at −25°, yielding 1.1 g. (36%) of fine white solid, m.p. 188–190° (subl. 155°) (Fisher–Johns melting point block). Recrystallization from water at 2° yielded 0.8 g. of pure aminohendecanoic acids, m.p. 186–187° (subl. 164°) [literature[9] m.p. 176°, for 11-aminohendecanoic acid].

Anal. Calcd. for $C_{11}H_{23}NO_2$: C, 65.6; H, 11.5; N, 6.96. Found: C, 65.2; H, 11.5; N, 6.83.

12-Hydroxyformamidostearic Acids.—These were prepared from 14.9 g. (0.05 mole) of ricinoleic acid, 12 ml. (0.3 mole) of hydrogen cyanide and 45 ml. (0.7 mole) of 85% sulfuric acid at 20–30°. Mixing was accomplished in five minutes and stirring was continued for an additional hour. The reaction product was insoluble in ether; *n*-butyl alcohol was used for extraction. The product was dark amber and weighed 15 g. (84%).

Anal. Calcd. for $C_{19}H_{37}NO_4$: N, 4.08; S, 0; acid number, 163; sapn. number, 163. Found: N, 3.71; S, 0.50; acid number, 160; sapn. number, 182.

Discussion

Hydrogen cyanide adds readily to the double bond of oleic, 10-hendecenoic and ricinoleic acids to give moderate to high yields of the anticipated formamido acids.

Either 85% sulfuric acid (reaction time two hours) or 95% sulfuric acid (reaction time 15 minutes) was used depending on the size of the reaction. In the large runs, the former concentration was preferred because mixing could not be accomplished in so short a time. Long reaction times with 95% sulfuric acid yielded amido acids containing appreciable amounts of sulfur. The ratio of reactants previously employed,[2] namely, 1 mole unsaturated compound:3 moles hydrogen cyanide:6 moles sulfuric acid, was satisfactory. In some instances, larger ratios of hydrogen cyanide were used merely to ensure an adequate excess, since it is known to decompose in concentrated sulfuric acid.

As was expected, formamido acids are hydrolyzed about 25 times faster than are the corresponding acetamido acids.[2] A minimum concentration of sulfuric acid of 10% was required. No difference in rate of hydrolysis, as measured by production of formic acid, was noted with 10 or 50% sulfuric acid. With formamidohendecanoic acids, however, a sulfuric acid concentration of 50% caused rapid decomposition of the product, whereas with 10% sulfuric acid hydrolysis to aminohendecanoic acid sulfates proceeded smoothly. On the other hand, with formamidostearic acids, aminostearic acid sulfates were obtained only when 50% sulfuric acid was employed.

Amino acid sulfates were easy to crystallize and could be isolated in good yield. Hydrolysis of 12-hydroxyformamidostearic acids to the amino acid sulfates could not be accomplished. The hydrolysis products contained only about 30% of the expected nitrogen content.

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(9) British Patent 591,027 (1947).

Difficulty was experienced in obtaining pure aminostearic and aminohendecanoic acids from the corresponding sulfates, although yields of crude amino acids were high. The reasons for this are not known. Possible explanations are the difficulty in finding the point of exact neutralization and the mixture of isomers may be more complex than that obtained when acetonitrile,[2] rather than hydrogen cyanide, is added to the double bond. Acetic acid is not as satisfactory as hydrochloric acid for neutralization of the solution of the amino acid sulfates in aqueous alkali since ash-free products could not be obtained. Solution of aminostearic acid sulfates in an excess of ammonia followed by boiling off of the ammonia did not give the amino acids alone but yielded mixtures of the free amino acid and its sulfates.

Reaction of hydrogen cyanide with linoleic acid resulted in some addition, but no identifiable products could be isolated. The high viscosity of the reaction product suggested that polymerization, caused by sulfuric acid, predominated.

Philadelphia, Penna.

[Contribution from the Department of Entomology, University of California, Citrus Experiment Station]

Insecticidal Action of Esters and Ethers of 2,2,2-Trichloro-1-(*p*-chlorophenyl)-ethanol[1]

By Martin J. Kolbezen, Francis A. Gunther, Roger C. Blinn and Glenn E. Carman

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The acaricidal activity of 2,2,2-trichloro-1-(*p*-chlorophenol)-ethanol gave an opportunity to study the effect of the hydroxyl group in the toxic action of this compound. Fifteen ester and ether derivatives, nine of them new, of this compound were synthesized and bioassayed against four species of insects and one species of mite. In this manner the effects of the reduction of polarity of the hydroxyl group upon penetration and transport and the possible hydrolysis of the esters could be studied. No marked differences in toxicity were noted in the experiments with the mite and with the three species of insects, but a specificity of certain compounds was observed for the confused flour beetle.

In order to be effective, a contact insecticide must be able to penetrate insect cuticle and subsequently reach the site of action where the penetrated molecule then exerts its biochemical effect with both primary and secondary actions.[2] In a previous paper,[3] the role of the ring in Ring-$CH_2OH{\cdot}CCl_3$ compounds in insecticidal action was briefly discussed; against mosquito larvae, *Culex quinquefasciatus* Say, and greenhouse thrips, *Heliothrips haemorrhoidalis* (Bouché), such rings appeared to function primarily[2] as spacers with polarizable characteristics.

As discussed previously,[3] compounds of the 2,2,2-trichloro-1-arylethanol type are synthetic precursors of the DDT-type molecule, yet they have demonstrable insecticidal and acaricidal activity.[4,5] Of a series of compounds containing a single *p*-chlorophenyl group, 2,2,2-trichloro-1-*p*-chlorophenylethanol was found to be the most effective.

Since esters are in general lipoid soluble, some aliphatic esters of this compound, varying in chain length and isomerism, were prepared to attempt enhancement of penetration and transport by alteration of the polar hydroxyl group. During the course of this investigation the *n*-butyrate was found to be the most effective of the *n*-esters against the confused flour beetle, *Tribolium confusum* Duv.; therefore, its isomer and isomers of higher esters were also included. To determine whether hydrolysis of the esters during transport or at the site of action occurred, some homologous ethers of this same ethanol were prepared.

Several investigators have prepared other miscellaneous esters and ethers of this alcohol for insecticidal evaluation.[6] Neither their compounds nor the parent alcohol were found to be as effective as DDT and certain of its analogs against several insects. Our compounds synthesized by standard methods are shown in Table I along with pertinent physical and analytical data.

These ester and ether derivatives were bioassayed against four species of insects and one species of mite. The insect and mite assays, except for that of the confused flour beetle, were made by standard methods as previously reported.[7]

Bioassays with the latter species were made by confining adult beetles in whole-wheat flour adulterated with the test compounds. Percentage-by-weight mixtures (5% for this test) were prepared by careful and thorough blending with mortar and pestle, and five grams of each mixture was placed in each of four one-ounce seamless salve tins. Twenty adult beetles selected at random from a mass culture of the confused flour beetle were placed in each container, and mortality determinations were made at the end of 24-, 72-, 168- and 360-hour exposures.

Discussion

The toxicity data for mosquito larvae exhibited an LD_{50} concentration, which ranged from 1×10^{-2} M to 2×10^{-3} M, and demonstrated an approximately equal toxicity for all the compounds. The

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