Formation and Mass Spectral Fragmentation of Ritter Products from Some Monoenic Fatty Acids. Location of Double-Bond Position in Unsaturated Acids

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By modification of the known Ritter conditions for making N-substituted amides by addition of acrylonitrile to olefinic compounds, it is possible to apply this reaction to new monoenic fatty acids. Procedures are presented for the addition of acrylonitrile to oleic acid (**2a**), methyl *cis*-5-eicosenoate (**3**), erucic (**4**), and brassidinic (**5**) acids, and the addition of acetonitrile to brassidinic acid. Yields of 54 to 80–84% of the respective monoacrylamides (**10–12**) and acetoamide (**8**) were obtained in crystalline form from the monoenic fatty acids by applying the proper ratio of reactants and by the mode of addition. Evidence is adduced, showing that it is possible to determine the addition sites in the Ritter products by mass spectrometry, and also that mass spectral analysis of Ritter products from olefinic compounds could be of general utility for the assignment of double bond position in the carbon chain.

The formation of acylamino fatty acids of structure $CH_3[CH_2]_xCH(NHCOR)[CH_2]_yCOOR'$ by interaction of nitriles and monoenic acids in the presence of strong acids (designated the Ritter reaction) is well documented.[1-6]

Earlier investigators in the fatty acid field have noted that the C_{18}-monoenic acids, oleic (**2a**)[2b] and petroselinic (**1**),[2c] lend themselves to smooth Ritter reaction with a variety of saturated and unsaturated aliphatic nitriles, dinitriles,[3] and hydrogen cyanide, but in no case was the position of the addition determined.

With the exception of **1** → **6** and **2** → **7** conversions, reactions of acrylonitrile with some other monoenic fatty acids do not appear to have been studied. Our interest in such a study emerged from a research project aimed at exploring the ability of Ritter-type products (**6–7**, **10–12**) from acrylonitrile to undergo the Diels–Alder reaction.[7]

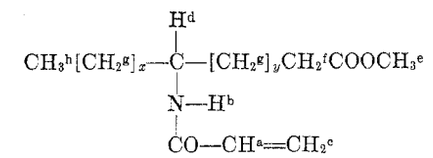
We have presented here the application of the Ritter reaction to a variety of pure homologs of long-chain unsaturated acids in the C_{18} to C_{22} range (see Scheme I) and results of a mass spectral study of the Ritter products **7–12**.

Results of the Ritter Reaction.—The procedures and results of the Ritter reaction between acrylonitrile and a series of monoenic fatty acids described here relate to the following substrates: oleic (**2a**), *cis*-5-eicosenoic (**3**), *cis*-13-docosenoic (erucic **4**), and *trans*-13-docosenoic (brassidinic, **5**) acids. We also included in this study the reaction between acetonitrile and **2b**, and the catalytic reduction of methyl acrylamidostearate (**9**) into methyl propionamidostearate (**10**).

The experimental part describes the series of experiments which give the optimum yields of once-recrystallized material obtained from a series of reactions in which variations in the ratio of reactants and in the mode of addition were studied. Other features were determined after three or more recrystallizations from acetone.

Satisfactory yields of methyl *N*-acrylamidostearate (**9**) were obtained when concentrated sulfuric acid was added to a mixture comprised of oleic acid–acrylonitrile–H_2SO_4 in a ratio of 1:3:3, with a reaction time of 45–60 min at 27–30°. Reasonable yields of the respective acrylamide, methyl acrylamidobehenate (**12b**), and methyl acetamidobehenate (**8**) were obtained in the cases of *cis*- and *trans*-13-docosenoic acids (erucic and brassidinic acid, **4** and **5**, respectively) when a ratio of fatty acid–nitrile–H_2SO_4 of 1:1.2:6 was employed under similar reaction conditions. The highest yield (80%) of an acrylamide (**11**) was obtained from the reaction of acrylonitrile with methyl *cis*-5-eicosenoate (**3**), the double bond of which appears to be relatively highly reactive towards the Ritter reaction.

The ir spectra of the Ritter products showed strong absorption at 3250–3300 and 1610–1625 cm^{-1}, corresponding to the amide group. In addition, these compounds also exhibited bands at 1650–1660, 972–987, and 947–965 cm^{-1} due to the vinyl group conjugated with a carbonyl.



The nmr spectral parameters of **7**, **9**, **11**, and **12** in $CDCl_3$ are essentially the same. As expected, the protons attached to the long carbon chain resonate between τ 6.0 and 9.12 [τ 6.05 (1 H, m, H^d), 6.35 (3 H, s, H^e), 7.70 (2 H, t, J = 7 Hz, H^f), 8.2–9.0 (H^g), and 9.12 (3 H, t, J = 5 H_z, H^h)], whereas the resonances of protons attached to the acrylamido group are only slightly affected by the environment, as follows: 3.75 τ (1 H, d, H^a), 4.38–4.50 (2 H, d, H^c), and 4.05–3.48 (1 H, d, J = 9 Hz, H^b).

Experimental Section

Materials and Sources.—The sources for the purchased chemicals are given in parentheses. Oleic acid (**2a**) (Nutritional Biochemicals Corp.), methyl oleate (**2b**) (British Drug House), *trans*-13-docosenoic (brassidinic acid, **5**) (Fluka, A.G.), *cis*-13-docosenoic (erucic acid, **4**) (Fluka), ethyl linoleate (**7b**) (Fluka), and acrylonitrile (British Drug House) were of "chemically pure" grade. Acrylonitrile, bp 72–73° (690 mm), was distilled under nitrogen atmosphere before use. Silicic acid (100 mesh) for chromatography (Mallinckrodt) was of analytical grade.

Isolation of *cis*-5-Eicosenoic and *cis,cis*-5,13-Docosadienoic Acids from *Limnanthes douglasii* Seed Oil.—The major compo-

(1) Deceased.

(2) (a) L. I. Krimen and D. J. Cota, *Org. React.*, **17**, 213 (1969); (b) E. T. Roe and D. Swern, *J. Amer. Chem. Soc.*, **75**, 5479 (1953); (c) *ibid.*, **77**, 5408 (1955).

(3) A. E. Kulikova, S. B. Meiman, and E. N. Zilberman, *Chem. Abstr.*, **59**, 11240e (1963).

(4) R. L. Holmes, J. P. Moreau, and G. Sumrell, *J. Amer. Oil Chem. Soc.*, **42**, 922 (1965).

(5) G. Jansen and W. Taub, *Acta Chem. Scand.*, **19**, 1772 (1965).

(6) L. W. Hartzel and J. J. Ritter, *J. Amer. Chem. Soc.*, **71**, 4130 (1949).

(7) S. Blum, S. Gertler, S. Sarel, and D. Sinnreich, submitted for publication.

SCHEME I

$$\underset{\textbf{1–5}}{CH_3[CH_2]_mCH{=}CH[CH_2]_nCOOR} + R''CN \xrightarrow{H^+,\ ROH} \underset{\textbf{6–12}}{CH_3[CH_2]_xCH(NHCOR'')[CH_2]_yCOOR}$$

1, R = H; $m = 10$; $n = 4$
2a, R = H; $m = n = 7$
2b, R = CH_3; $m = n = 7$
3, R = CH_3; $m = 13$; $n = 3$
4, R = H; CH=CH (cis); $m = 7$; $n = 11$
5, R = H; CH=CH (trans); $m = 7$; $n = 11$

6, R = H; R'' = $CH{=}CH_2$; $(x + y) = 15$
7, R = H; R'' = $CH{=}CH_2$; $(x + y) = 15$
8, R = R'' = CH_3; $(x + y) = 15$
9, R = CH_3; R'' = $CH{=}CH_2$; $(x + y) = 15$
10, R = CH_3; R'' = C_2H_5; $(x + y) = 15$
11, R = CH_3; R'' = $CH{=}CH_2$; $(x + y) = 17$
12, R = CH_3; R'' = $CH{=}CH_2$; $(x + y) = 19$

nents of the seed oil are: *cis*-5-eicosenoic acid ($C_{20}H_{38}O_2$, 65%), *cis*-13-docosenoic (erucic) acid ($C_{22}H_{42}O_2$, 13%), *cis*-5-docosenoic acid ($C_{22}H_{42}O_2$, 7%), and *cis,cis*-5,13-docosadienoic acid ($C_{22}H_{40}O_2$, 11%).[8] The predominant C_{20}-monoenic and the minor C_{22}-dienoic acids were obtained by way of fractional crystallization at −60° followed by separation between the mercuric acetate adducts, according to the procedure of Fore, *et al.*[9] The separation between the two C_{22}-monoenic acids was troublesome. In the vpc a mixture of these acids exhibits a single peak.

Methyl *cis*-5-eicosenoate (5) had bp 185–187° at 2 mm (lit.[9] bp 180–182° at 1 mm), was of 90–95% purity (vpc analysis with a 10-ft by 0.25-in. width column filled with 20% stabilized DEGS on 60–80 Chromosorb W, at 245°), and was obtained in 40–45% yield.

Acrylamido Fatty Acids and Derivatives. Application of the Ritter Reaction.—Procedure and **Results** are given for additions of acrylonitrile to oleic (**2a**), *cis*-13-docosenoic (erucic) (**4**), *trans*-13-docosenoic (brassidinic) (**5**), and *cis*-5-eicosenoic (**3**) acids. The reaction in sulfuric acid was generally started at or below 0°, according to the tendency of the unsaturated compound to undergo the Ritter reaction, and then was allowed to warm up. The reaction was completed at 27–30° for *ca.* 1 hr, followed by addition of methanol or ice water.

Methyl Acrylamidostearate (9).—The procedure described below represents the optimal conditions for generation of the title compound from oleic acid.

A mixture of 28.2 g (0.1 mol) of **2a** and 15.9 g (0.3 mol) of freshly distilled acrylonitrile was well stirred and cooled to −20° (ice–salt) while 33.8 g of H_2SO_4 (95%) was added dropwise in such a rate as to maintain the internal temperature around 27° (about 20 min). This was then stirred for 1 hr at room temperature, and then poured into 200 ml of cold methanol and allowed to stand overnight. The esterification was completed by refluxing the mixture for 2.5 hr and the excess methanol was removed at reduced pressure. The residue was extracted by ether, thoroughly washed with water, 5% aqueous sodium bicarbonate, and saturated sodium chloride solution, and dried. Removal of ether furnished 31.5 g of an oily residue which, on trituration with petroleum–ether (40–60°), yielded 22.7 g (62%) of crystalline methyl acrylamidostearate of mp 37–42°. Successive recrystallizations of the product from ethanol at −70° raised the melting point to 72–77°. Its ir spectrum exhibited peaks at 3255 (NH), 1736 (CO ester), 1622 (amide), 1652, 982, and 945 cm^{-1} ($CH{=}CH_2$).

Acrylamidostearic Acid (7).—In a typical experiment, 0.4 mol of concentrated sulfuric acid (98%) was added dropwise to a well-stirred mixture of **2a** (0.1 mol) and freshly distilled acrylonitrile (0.11 mol) at 0° during 30 min. The mixture was allowed to warm to 27–30° for 30 min and then was carefully poured with stirring into ice water. Stirring was continued for 16 hr, resulting in a homogeneous viscous mass which was then extracted with ether. The extract was washed with 5% sodium bicarbonate and dried ($MgSO_4$), and solvent was removed. The brown oily residue (7.1 g, 20%) was chromatographed on a silica column (350 g), using ether as eluting solvent, providing a colorless low-melting solid product. Recrystallization from acetone at −70° yielded microcrystals of **7** [mp 35–40° (lit.[2a] viscous oil); ir (KBr) 3250, 1705, 1620, 1650, 983, and 950 cm^{-1}], which analyzed as a $C_{21}H_{39}NO_3$ product.

Acrylamidostear-*p*-toluidide.—A mixture of **7** (0.52 g) and *p*-toluidine (1 g) was heated to 190–210° for 2 hr, and then was cooled. The mixture was extracted by ether, washed with 10% hydrochloric acid and water, and dried, and the solvent was removed. Recrystallization from aqueous ethanol provided 0.12 g (18%) of colorless crystals of the *p*-toluidide, mp 125–135°.

Anal. Calcd for $C_{28}H_{46}N_2O_2$: C, 76.0; H, 10.5; N, 6.3. Found: C, 76.0; H, 10.6; N, 6.4.

Acrylamidostearanilide, mp 63–65°, was similarly prepared from **7** (1.1 g) and aniline (1 g) in 16% yield.

Methyl Acrylamidobehenate (12b). i. From *trans*-13-Docosenoic (Brassidinic) (5) Acid.—In a manner described above, a mixture of 13.5 g of **5** and 6.36 g of acrylonitrile was well stirred and cooled in an ice–salt bath, while 13.5 ml of 98% H_2SO_4 was added dropwise during 30 min. The mixture was then allowed to warm up for 30 min and finally was poured into cold methanol with continual stirring. After the work-up, as described above, 15.4 g of an oily product (**12b**) was obtained. It was eluted with petroleum ether (60–80°) and finally recrystallized from ethanol at −60°, mp 55–70°. An analytial sample of methyl acrylamidobehenate (**12b**) of mp 73–77°, which analyzed as a $C_{25}H_{49}NO_3$ product, could be obtained after several recrystallizations.

ii. From *cis*-13-Docosenoic (Erucic) Acid (4).—The reaction of erucic acid (0.1 mol) and acrylonitrile (0.25 mol) in the presence of 98% H_2SO_4 (27 ml) in a fashion described above afforded methyl acrylamidobehenate (53%): mp 73–77°; ir 3254, 1737, 1622, 1653, 982, and 947 cm^{-1}.

Acrylamidobehenic Acid (12a). From *trans*-Docosenoic (Brassidinic) Acid.—To a mixture of **5** (20 mmol) and acrylonitrile (24 mmol) was added dropwise 98% H_2SO_4 (120 mmol) during 30 min, at −20°. The mixture was treated in a manner described above. Column chromatography (silica gel) followed by successive recrystallizations from acetone at low temperature furnished colorless crystals (42–45%) of acrylamidobehenic acid (**12a**) (mp 55–70°; ir 3250, 1711, 1622, 1655, 985, and 954 cm^{-1}), which gave the correct elemental analysis for $C_{25}H_{47}NO_3$.

Methyl Acrylamidoeicosanoate (11). The Ritter Reaction of Methyl *cis*-5-Eicosenoate (3).—A well-stirred mixture of methyl *cis*-5-eicosenoate (**3**) (6.5 g, 0.02 mol) and acrylonitrile (3.2 g, 0.06 mol) was cooled to 0°, 6.3 ml of 98% H_2SO_4 being added dropwise during 30 min, finally poured into 20 ml of cold methanol, and left to stand for 16 hr at room temperature. It was then poured onto ice, extracted with ether, washed, and dried, and the solvent was removed. The crude methyl acrylamidoeicosanoate (**11**) was obtained in 80% yield. The pure product was obtained by vapor phase chromatography on a 2-ft column packed with silica gum rubber SE-30 on Chromosorb W 60–80 mesh reg, followed by recrystallization from acetone: mp 71–74°; R_f 0.39–0.42 [tlc, on Kieselgel, chloroform–methanol (24:1) as eluent]; ir 3300, 1740, 1620, 1650, 9.72, and 960 cm^{-1}. It gave the correct elemental analysis for $C_{25}H_{47}NO_3$.

Methyl Acetamidobehenate (8).—In the fashion described above, a mixture of 2.7 g of **5** and 1 g of acetonitrile was treated with 2.7 ml of 98% H_2SO_4 at 0° during 30 min, and, before the reaction mixture was quenched in cold methanol, it was allowed to warm up for 30 min. After the usual work-up the Ritter product **8** was obtained in crystalline form (51%), mp 69–74° (from ethanol).

Anal.. Calcd for $C_{25}H_{49}NO_3$: C, 73.0; H, 11.9; N, 3.31. Found: C, 72.7; H, 11.8; N, 3.0.

Preparation of Methyl Propioamidostearate (10). The Catalytic Reduction of 9.—Into a Parr instrument bottle was placed a solution of 0.8 g of methyl acrylamidostearate (**9**) [mol wt 367 (mass spectra)] in 50 ml of ethanol and 50 mg of 5% Pd/C, shaken with hydrogen for 2 hr. After the usual work-up, crystals (85%) of methyl propionamidostearate (**10**) were obtained. Recrystallization from ethanol afforded white crystals of mp 57–61°, mol wt 369 (mass spectra), analyzed as $C_{22}H_{43}NO_3$ product,

(8) M. O. Ragby, C. R. Smith, T. K. Miwa, R. L. Lohmer, and I. A. Wolff, *J. Org. Chem.*, **26**, 1261 (1961).

(9) S. P. Fore, F. G. Dollear, and G. Sumrell, *Lipids*, **1**, 73 (1966).

displaying the characteristic bands at 3230 (NH), 1680 (C=O ester), and 1580 cm^{-1} (C=O amide), the disappearance of the vinyl stretching vibration at 1652 cm^{-1}, and the deformation vibrations at 982 and 945 cm^{-1}, in ir spectrum.

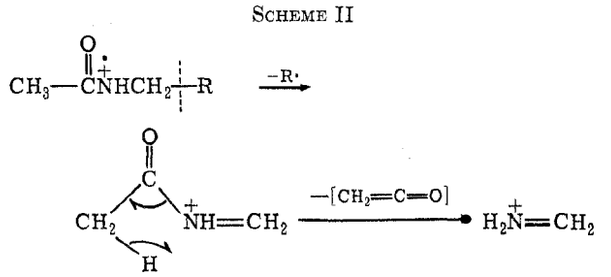
Determination of Addition Positions in Ritter Products by Mass Spectrometry

The physical properties of the Ritter product from acrylonitrile and oleic acid have been discussed earlier[2a] in terms of the formation of an isomeric mixture. To establish isomeric distribution in Ritter products from 1-octadecene and a variety of nitriles, Clarke, *et al.*,[10] applied the vapor phase chromatographic technique (vpc) to the amines obtained after alkaline hydrolysis. They have encountered increasing difficulty in separating the isomers by vpc as the amino group becomes more remote from the terminal position.

In order to determine the addition positions in Ritter products from acrylonitrile and the monoenic fatty acids described above, a mass spectral study of these products was undertaken.

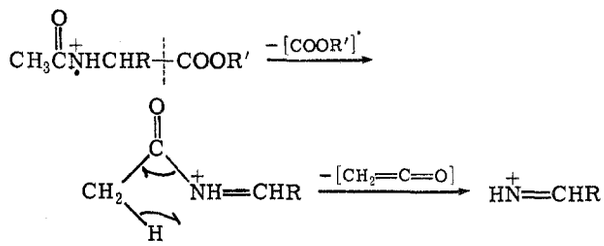
The mass spectral analysis was based on the well-known observation evidenced in a thorough mass spectral study of *N*-butylacetamide[11] that the principal electron-induced fragmentation of secondary amides involves rupture of the C–C bond α to the amido function, with charge retention on the latter. This fragment then loses a methylene ketene molecule by cleavage of the CO–N bond with hydrogen rearrangement to give iminium ions[12] (see Scheme II).

SCHEME II



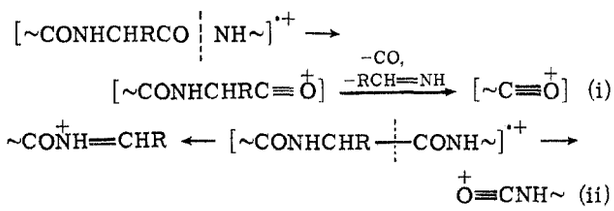
The mass spectra of *N*-acetylamino acids[13] and their alkyl esters[14] all show an intense acetyl ion (*m/e* 43), and the chief common feature is loss of the carboxyl (or alkoxycarbonyl) group to give an acyliminium ion, which then ejects methyleneketene with formation of an amine fragment (Scheme III). Ionized peptide chains, on the other hand, rupture at the amide bonds in two main modes:[15] (i) cleavage of the CO–N bond giving

SCHEME III



acylium ions which then lose carbon monoxide and a neutral imine fragment, and (ii) cleavage of the C–CO bond with retention of charge by either moiety (Scheme IV).

SCHEME IV



On the basis of this knowledge one might expect that, upon electron impact, the fragmentation of N-substituted fatty acrylamides of structures **9** and **11**–**12** would be very characteristic, which would permit the deduction of addition site in the Ritter products from the respective unsaturated fatty acids **2**, **3**, and **4**–**5**.

The mass spectra were measured on the Atlas MAT CH4 mass spectrometer using the direct inlet system. The electron energy was maintained at 70 eV and the ionization current was maintained at 20 μA. The abundances of ions from primary fragmentations are given in percentages relative to the *m/e* 55 peak ion (CH_2=$CHCO^+$) and assembled in Tables I–V.

In the mass spectra of all unsaturated Ritter products (**9**, **11**, and **12**) the ion of highest mass-to-charge ratio is the acryl ion, CH_2=CHC^+≡O (*m/e* 55) (see Tables I, III, and V), whereas in methyl propionamidostearate (**10**), resulting from **9** → **10** conversion, and also in methyl acetamidostearate (**8**), the most intense peak is *m/e* 74 (see Tables II and IV). This corresponds to the $C_5H_6O_2^+$ fragment, which is the predominant peak in the mass spectra of methyl stearate,[16] and to which the structure CH_2=$C(OH)OCH_3$ was assigned. It probably results from McLafferty rearrangement as depicted in Scheme V.

In analogy to secondary aliphatic amides and to esters of fatty acids, the most prominent peaks in the mass spectra of **8**–**12** correspond to ions of structures **13**–**17**, resulting from α cleavages at both sides of the C–N bond (fragmentations of type A and B),[17] which upon expulsion of either a C_3H_2O unit (conversions of **14** to **16** and of **13** to **15**) or alcohol from the acid moiety (rupture of **14** to **17**) give rise to the iminium ions **15** and **16** and the acylium ion **17** (Scheme VI).

(10) T. Clarke, J. Devine, and D. W. Dicker, *J. Amer. Oil Chem. Soc.*, **41**, 78 (1964).

(11) (a) Z. Pelah, M. A. Kielczewski, J. M. Wilson, M. Ohashi, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 2470 (1963); (b) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Chapter 9, Holden-Day, San Francisco, Calif., 1967, pp 338–339.

(12) E. Breuer, S. Sarel, A. Taube, and J. Sharvit, *Isr. J. Chem.*, **6**, 777 (1968).

(13) K. Heyns and H. F. Grützmacher, *Justus Liebigs Ann. Chem.*, **667**, 194 (1963).

(14) C. O. Andersson, R. Ryhage, and E. Stenhagen, *Ark. Kemi*, **19**, 417 (1962).

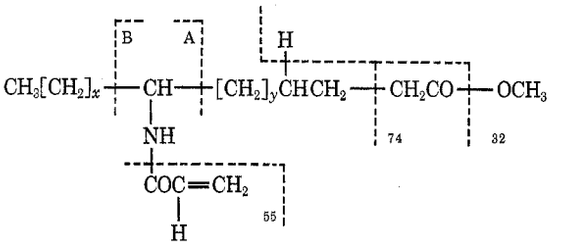
(15) (a) K. Heys and H. F. Grützmacher, *Justus Liebigs Ann. Chem.*, **669**, 189 (1963); (b) M. M. Shemyakin, Yu. A. Ovchinnikov, A. A. Kiryushkin, E. J. Vinogradova, A. I. Miroshnikov, Yu. B. Alakhov, V. M. Lipkin, Yu. B. Shetsev, N. S. Wulfson, B. V. Rosimov, V. N. Bocharev, and V. M. Burikov, *Nature (London)*, **211**, 361 (1966); (c) F. Weygand, A. Prox, H. H. Fessel, and K. K. Sun, *Z. Naturforsch., B*, **20**, 1169 (1965); (d) E. Bricas, J. Van Heijenoort, M. Barber, W. A. Wolstenholme, B. C. Das, and E. Lederer, *Biochemistry*, **4**, 2254 (1965).

(16) (a) Ng. Dinh-Nguyen, R. Ryhage, S. Stallberg-Stenhagen, and E. Stenhagen, *Ark. Kemi*, **18**, 393 (1961); (b) K. K. Sun and R. T. Holman, *J. Amer. Oil Chem. Soc.*, **45**, 810 (1968).

(17) (a) W. Vetter, P. Longevialle, F. Khuong-Huu-Laine, Q. Khuong-Huu, and R. Goutarel, *Bull. Soc. Chim. Fr.*, 1324 (1963); (b) L. Dolejs, V. Hanus, V. Cerny, and F. Sorm, *Collect. Czech. Chem. Commun.*, **28**, 1584 (1963); (c) see ref 11a.

TABLE I

RELATIVE ABUNDANCE OF AMINE (A-54), AMIDE (A, B-32), AND ESTER PEAKS (B, B-54) IN THE MASS SPECTRUM OF METHYL ACRYLAMIDOSTEARATE (9)

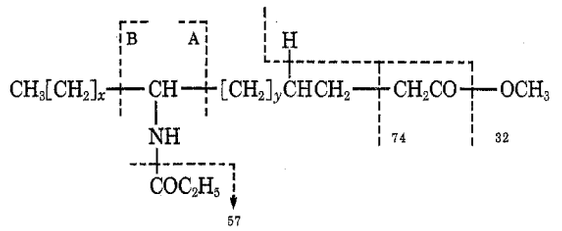


mol peak (m/e 366) = 3%; base peak (m/e 55) = 100%; ester peak (m/e 74) = 10%

Position of attachment	Peak A		A-54		B		B-32		B-54	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-7	238	6	184	4	212	7	180	5	158	2
C-8	224	19	170	13	226	19	194	13	172	4
C-9	210	65	156	32	240	50	208	30	186	9
C-10	196	66	142	33	254	50	222	31	200	9
C-11	182	15	128	9	268	6	236	5	214	2

TABLE II

RELATIVE ABUNDANCE OF AMINE (A-56), AMIDE (A, B-32), AND ESTER PEAKS (B, B-56) IN THE MASS SPECTRUM OF METHYL PROPIONAMIDOSTEARATE (10)

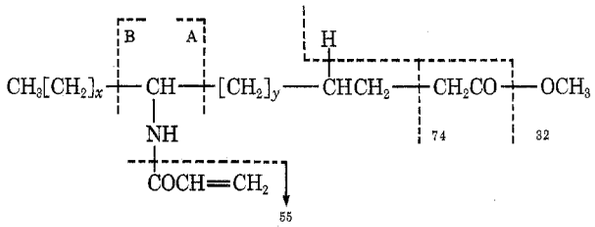


mol peak (m/e 369) = 14%; base peak (m/e 74) = 100%; peak (m/e 57) = 55%

Position of attachment	Peak A		A-56		B-32		B		B-56	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-7	240	6			182	5	214	15	158	6
C-8	226	22	170	43	196	6	228	32	172	24
C-9	212	48	156	80	210	18	242	57	186	52
C-10	198	50	142	80	224	18	256	50	200	52
C-11	184	22	128	13	238	3	270	7	214	15

TABLE III

RELATIVE ABUNDANCE OF AMINE (A-54), AMIDE (A, B-32), AND ESTER PEAKS (B, B-54) IN THE MASS SPECTRUM OF METHYL ACRYLAMIDOBEHENATE (12)

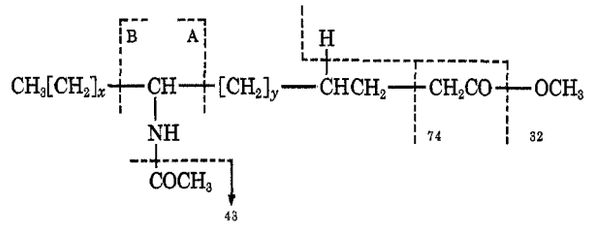


mol peak (m/e 423) = 22%; base peak (m/e 55) = 100%; peak (m/e 74) = 10%

Position of attachment	Peak A		A-54		B-32		B		B-54	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-11	238	6	184	1.5	236	3	268	1	214	1.5
C-12	224	16	170	3	250	3	282	4	228	1.5
C-13	210	98	156	63	264	31	296	74	242	9
C-14	196	95	142	65	278	32	310	75	256	9
C-15	182	8	128	1.5	292	1.5	324	5	270	1.5

TABLE IV

RELATIVE ABUNDANCE OF AMINE (A-42), AMIDE (A, B-32), AND ESTER PEAKS (B, B-42) IN THE MASS SPECTRUM OF METHYL ACETAMIDOBEHENATE (8)

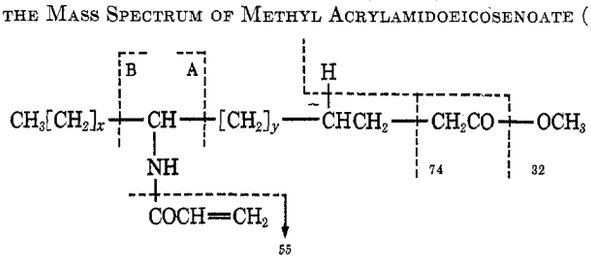


mol peak (m/e 411) = 9%; base peaks (m/e 74) = 100%, (m/e 43) = 98%

Position of attachment	Peak A		A-42		B-32		B		B-42	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-11	226	20			224	10	256	30	214	12
C-12	212	33			238	11	270	35	228	18
C-13	198	99	156	22	252	14	284	97	242	28
C-14	184	99	142	19	266	12	298	81	256	30
C-15	170	30	128	11	280	6	312	26		

TABLE V

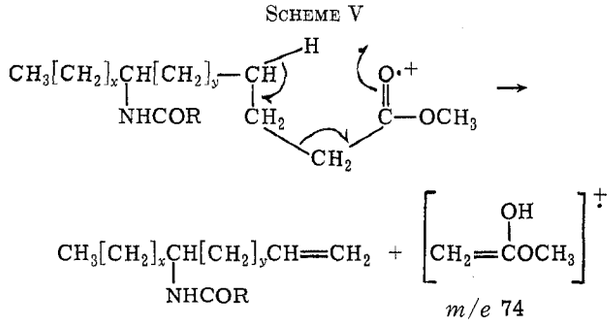
RELATIVE ABUNDANCE OF AMINE (A-54), AMIDE (A, B-32), AND ESTER PEAKS (B, B-54) IN THE MASS SPECTRUM OF METHYL ACRYLAMIDOEICOSENOATE (11)



mol peak (m/e 395) = 57%; base peak (m/e 55) = 100%; peak (m/e 74) = 13%

Position of attachment	Peak A		A-54		B-32		B		B-54	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-5	294	14	240	27	152	4	184	30	130	1
C-6	280	81	226	85	166	20	198	95	144	29
C-7	266	84	212	100	180	24	212	100	158	39
C-8	252	58	198	95	194	15	226	85	172	19
C-9	238	14	184	30	208	2	240	27	186	3

SCHEME V



8, R = CH_3; $(x+y) = 12$
10, R = C_2H_5; $(x+y) = 12$

This suggest that loss of a C_3H_2O unit from fragment **18**, where R″ equals CH_2=CH– (from ionized **9**, **11**, and **12**), should involve rearrangement of an inner vinylic hydrogen as formulated in Scheme VII.

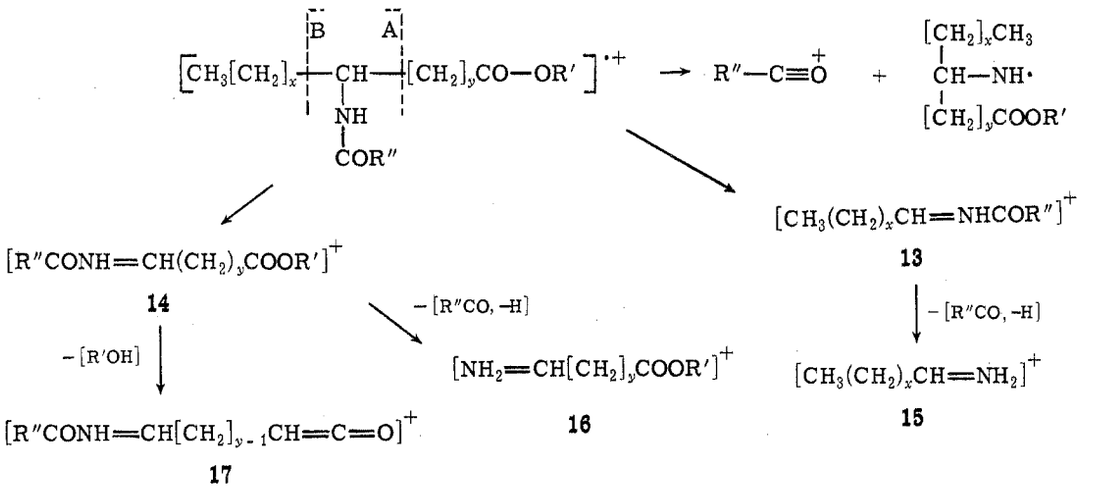
Like the pure homologs of long-chain acid esters,[16,18] the relative abundance of molecular ions in the mass spectra of **9**–**12** remarkably increases as the fatty carbon chain increases (compare Tables I, III, and V).

Examination of mass spectral data assembled in Tables I–V reveals that the most prominent peaks in the fragmentation of **8**–**10** and **12** are characterized by their appearance in pairs of equal intensity which are 14 mass units apart. Thus, in the mass spectra of **12** (Table III), they are m/e 156–142, 210–196, 242–256, 264–278, and 296–310, corresponding to fragments resulting from the primary reaction (cleavages A and B, in Scheme VI) and the secondary reactions involving losses of a C_3H_2O unit as depicted in Scheme VII (fragments A-54 and B-54) or the expulsion of methanol to yield B-32. Simple analysis shows that these fragments could originate from a mixture of ionized molecules of structure **12**, where the acrylamido nitrogen is equally and predominantly attached to carbons 13 ($x = 8$; $y = 11$) and 14 ($x = 7$; $y = 12$) of the fatty acid carbon chain.

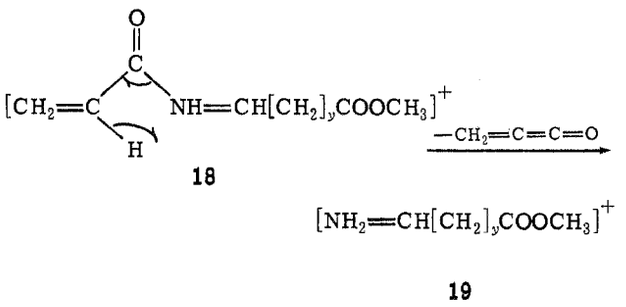
This suggest that the most favored carbonium ions from protonation of **4** or **5**, occurring in the course of Ritter reaction, are the secondary ones on C-13 and C-14, the isomerization of which to the C-12 and C-15

(18) (a) R. Ryhage and E. Stenhagen, *Ark. Kemi*, **13**, 523 (1959); (b) R. Ryhage, *ibid.*, **13**, 475 (1959).

SCHEME VI



SCHEME VII

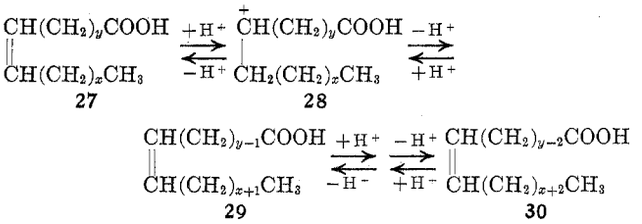


carbonium ions (which presumably generate products **12** where $x = 9$, $y = 10$, or $x = 6$, $y = 13$, respectively) is very small indeed.

The case is similar for the Ritter product **9** which emerges from the reaction of oleic acid with acrylonitrile. Its mass spectral analysis reveals that the entering acrylamido group favors an attachment either to C-9 or to C-10 (see Table I) and to a much lesser extent also to C-8, probably through equilibria between the various carbonium ion species.

Mass spectral analysis of **11** (Table V) shows that the isomeric distribution in the latter is relatively much broader. Under strong acidic conditions *cis*-5-eicosenoic acid (**3**) undergoes attack by acrylonitrile at carbons 6, 7, and 8 (at the carbonium ions **24**, **25**, and **26**, respectively; see Scheme VIII) rather than at the expected ones, 5 and 6 (**20** and **21**, respectively). An entrance of the acrylamido group has not been observed at carbons 2, 3, or 4. This can be explained, at least partly, in terms of formation of a γ-lactone intermediate[9] (**23**) which hinders isomerization of **20**, the first protonated species of **3**, toward the carboxyl group. Thus, the Ritter product **11** comprises an isomeric mixture mainly of **11ii**, **11iii**, and **11iv**, and to a much smaller extent of **11i** and **11v** (**11**, $x = 10$, $y = 7$).

The variation in isomeric distribution between the Ritter products from the various monoenic acids may be related to the reactivity of the specific carbonium ion species toward the acrylonitrile. Thus, the greater the reactivity of the carbonium ion species, the less is isomerization of the double bond of the type **27** → **30**, as shown in the following series of equations.



Hence, the additions in such cases should occur essentially on either carbon of the original double bond to yield 1:1 mixtures of the corresponding positional isomers. However, in the presence of a less reactive nitrile (acetonitrile), the initial protonated species of a monoenic acid appear to undergo isomerization prior to fruitful reaction with the nitrile. Indeed, mass spectral analysis of Ritter product **8** from the reaction of **5** with acetonitrile shows that **8** comprises a more complex mixture of the respective positional isomers relative to **12** (compare data in Tables III and IV).

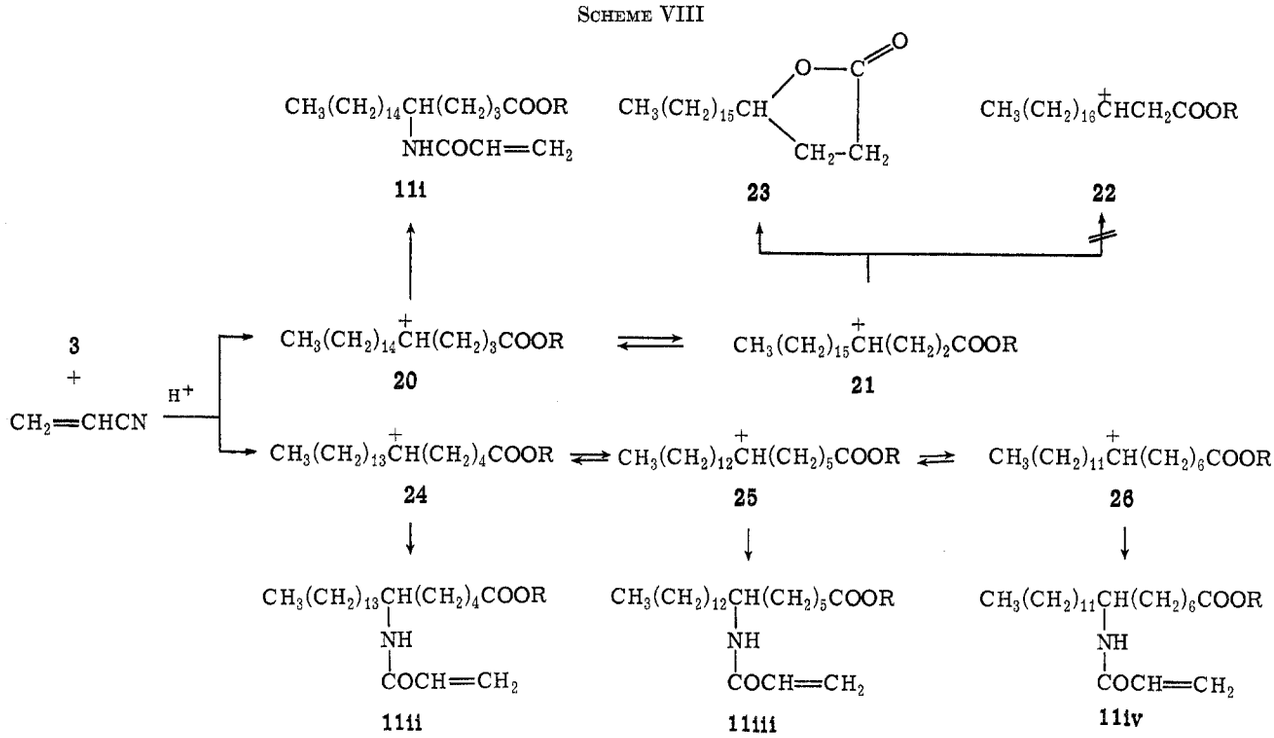
The differences in isomeric composition between the various Ritter products (**8**–**12**) suggest that their protonations give rise to highly reactive carbonium ions which collapse as soon as they are formed.

Following the evidence presented above we deemed it of interest to compare our data with that reported by Audier and coworkers,[19] who have shown that it is possible to locate the double bond position in a long-chain unsaturated compound by mass spectrometry.[20] This entailed first an epoxidation of the double bond and then treatment of the resulting epoxide with dimethylamine to afford the respective isomeric mixture of dimethylamino alcohols. Upon bombardment by high energy electrons the dimethylamino alcohols fragment to give, in addition to the base peak, two prominent peaks of similar intensity and 50% abundance relative to the predominant peak. Most significantly, the results obtained through application of Audier and coworkers' method for dimethyloleamide (**31**) compare remarkably well with those produced in this study for the oleic acid **2a** case (see Table II), as delineated in Scheme IX.

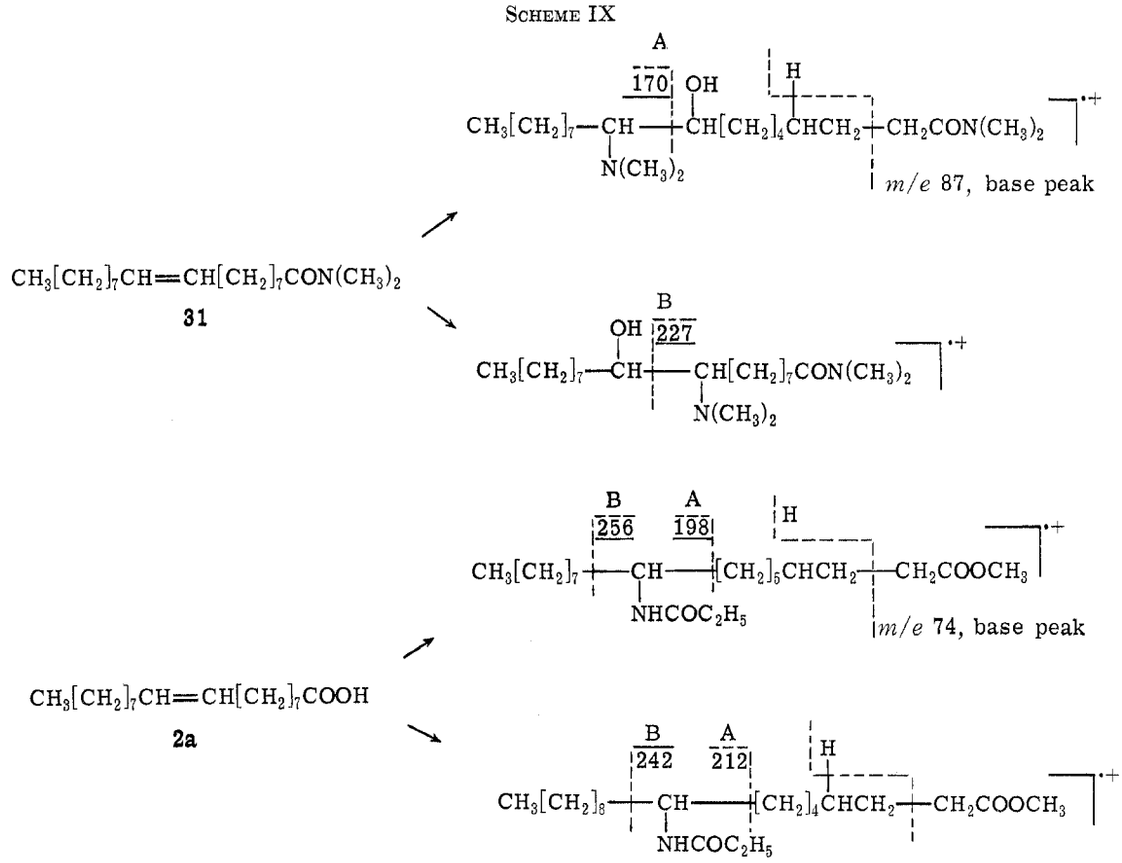
(19) H. Audier, S. Bory, M. Fetizon, P. Longevialle, and R. Toubiana, *Bull. Soc. Chim. Fr.*, 3034 (1964).

(20) See also (a) R. Ryhage and E. Stenhagen, *Ark. Kemi*, **15**, 545 (1960); (b) G. W. Kenner and E. Stenhagen, *Acta Chem. Scand.*, **18**, 1551 (1964).

SCHEME VIII



SCHEME IX



From the evidence presented here it follows that mass spectral analysis of Ritter products could be utilized conveniently as a tool in assigning the double bond position in a long-chain unsaturated compound.

Registry No.—**2a**, 112-80-1; **3**, 35053-79-3; **4**, 112-86-7; **5**, 506-33-2; **7**, 30995-39-2; **8**, 35025-51-5; **9**, 35025-52-6; **10**, 35025-53-7; **11**, 35025-54-8; **12a**, 35025-55-9; **12b**, 35025-56-0; acrylonitrile, 107-13-1; acrylamidostear-*p*-toluide, 35025-57-1; acrylamidostearanilide, 35025-58-2.

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