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

X-Ray Diffraction of Molecular Compounds of Long-chain Saturated Fatty Acids. II. Some Further Observations on the Diffraction of Molecular Compounds of Acetamide and Long-chain Saturated Fatty Acids

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RECEIVED MAY 20, 1957

Further examination of the X-ray diffraction patterns of molecular compounds of acetamide with myristic, palmitic and stearic acids has revealed the existence of two polymorphic forms. Three sets of long spacings have been identified: (a) a weak long spacing identical to that of the "C" form of the parent acid; (b) a shorter long spacing corresponding to a modification equal in length to one molecule of the "A" form of the saturated fatty acid and one molecule of acetamide; and (c) a longer long spacing corresponding in length to two molecules of the "C" form of the saturated fatty acid and two molecules of acetamide. Each of the polymorphic modifications of these three acetamide compounds has been shown to form an isomorphous series. The lauric acid addition compound is anomalous, exhibiting (other than the weak spacings identified as identical to those of the parent acid) only one set of spacings. This single set of spacings differs from the longer-chain homologs as it corresponds to one molecule of the "C" form of lauric acid and one molecule of acetamide and exhibits a considerably different pattern of short spacings. Long and short spacings, obtained by the usual powder technique are given in a tabulation. These data permit the identification of any of these addition compounds and of their polymorphic modifications.

In an earlier paper[2] it was shown that X-ray diffraction by the usual powder technique could be useful for the identification and differentiation of molecular compounds of acetamide and long-chain saturated fatty acids. Two long spacings were observed for the molecular compounds with lauric, palmitic and stearic acids, and three with myristic acid. One of the long spacings for each compound was of very weak intensity and was shown to be identical to the long spacing of the corresponding fatty acid. These spacings were accounted for by the presence of some free acid possibly due to sublimation of a small amount of acetamide from the fatty acid–acetamide addition compounds. The second set of spacings was considerably stronger and, with the exception of the stearic acid addition compound, showed good agreement with calculated spacings corresponding in length to a linear extension of two molecules of the "C" form of the acid and two molecules of acetamide. The appearance of a third long spacing for myristic acid could be explained on the plausible postulation of the presence of the unstable modification of this C_{14} acid previously described by Slagle and Ott.[3]

All long spacings were thus accounted for and, with the exception of that for the stearic acid compound, showed reasonable agreement with calculated values. The observed long spacing for the stearic acid molecular addition compound was 59.59 Å., the average of twelve reflection orders obtained from several patterns of different preparations. The calculated spacing on the basis of a 2:2 molecular addition compound of the "C" form of stearic acid and the long spacing for acetamide is 51.15 Å. This discrepancy, 8.44 Å., is at least tenfold greater than the precision with which the spacings can be measured and required further examination.

Additional investigations have revealed the existence of two polymorphic forms for the addition compounds with myristic, palmitic and stearic acids. The long spacings of one of these polymorphic modifications agree very well with calculations on the basis of a unit cell equal in length to one molecule of the long-chain fatty acid and one molecule of acetamide, both with the angle of tilt, 90°, established for the "A" form of the saturated fatty acids. The second polymorphic form has a unit cell equal in length to two molecules of the acids and two molecules of acetamide tilted at an angle of 59° 12′, characteristic of the "C" form of the parent acids. These two polymorphic forms will be referred to as the "A" and the "C" modifications of the addition compounds, corresponding to the "A" and "C" polymorphic forms of the long-chain saturated fatty acids.

Only one polymorphic form has been found for the lauric–acetamide compound. The observed X-ray long spacing for this compound is somewhat shorter than the value obtained by calculation from the shortest long spacing for lauric acid ("C" form) and acetamide. This addition compound differs from the "C" form of the C_{14}, C_{16} and C_{18} adducts in that its long spacing value indicates a 1:1 molecular addition compound of the "C" form of lauric acid and acetamide and its short spacings differ somewhat in pattern from those of its homologs.

Experimental

The polymorphic modification of the fatty acid–acetamide compound formed by fusion of the pure constituents differs with the fatty acid. That formed by solvent crystallization depends in addition upon the solvent and the concentration of the solution from which the crystals separate, and therefore upon the temperature at which they form. In general, the more concentrated solutions favored the formation of the "C" modification.

The following summarizes the procedures by which the two modifications of the specific fatty acid–acetamide compounds were prepared. All solvent crystallizations were performed in centrifugal filtration tubes.[4] The concentrations and solvent compositions given are on an approximate proportional weight basis.

The "C" form of the stearic acid compound was prepared by crystallization from a 2:1 benzene solution (2 parts of

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) R. T. O'Connor, R. R. Mod, M. D. Murray and E. L. Skau, THIS JOURNAL, **77**, 892 (1955).

(3) F. B. Slagle and E. Ott, *ibid.*, **55**, 4396 (1933).

(4) E. L. Skau, *J. Phys. Chem.*, **33**, 951 (1929); E. L. Skau and W. Bergmann, *J. Org. Chem.*, **3**, 166 (1938); E. L. Skau and H. Wakeham, "Melting and Freezing Temperatures," in Weissberger, "Physical Methods of Organic Chemistry," 2nd Ed., Interscience Publishers, New York, N. Y., 1949, Vol. I, Part I, pp. 99–100.

solute to one part of solvent); the "A" form was obtained by fusion of equimolar parts of acetamide and the acid, and by crystallization of an equimolar mixture from a 1:2 benzene solution or from acetone. The "C" form of the palmitic acid compound was obtained by crystallization from a 2:1 acetone solution; the "A" form was prepared by fusion and by crystallization from a 1:3 solution in a 1:2 acetone–benzene mixture. As previously reported[5] the stearic and palmitic acid compounds obtained by crystallization from acetone were contaminated with considerable free acid and gave a low nitrogen analysis. The "C" modification of the myristic acid compound was formed by fusion and by crystallization from a 3:1 acetone solution or from a 1:2 solution in a 1:1 acetone–benzene mixture; a second crop of crystals obtained from the mother liquor of the above crystallization from 1:1 acetone–benzene (estimated concentration 1:40) proved to be the "A" modification. For the lauric acid compound the "C" form was obtained by fusion and by crystallization from 1:1 acetone–benzene mixture; attempts to prepare the "A" form, even from very dilute solutions, were unsuccessful. In no case was there a perceptible difference in the melting points of pure samples of the "A" and "C" modifications.

It is apparent that the "C" modification of the lauric and myristic acid compounds tends to form more readily than the "A" modification, and that the reverse is true for the palmitic and stearic acid. This may possibly be connected in some way with the fact, shown by the binary freezing point diagrams of these acids with acetamide,[6] that the stearic and palmitic acid–acetamide compounds melt congruently while those for myristic and lauric acids can melt congruently or incongruently depending upon whether metastable or stable phase equilibrium is considered.

The X-ray measurements were made by the powder method previously described.[2]

Additional X-Ray Spacings.—In Table I average values of the long spacings of the addition compounds of acetamide and lauric, myristic, palmitic and stearic acids are listed. In the second column are the average values of the weaker spacings which have been identified as pertaining to traces of the free fatty acids.[2] The figures in parentheses are the most recently published values for the long spacings for the "C" forms of the free acids.[7] The excellent agreement between these and the experimentally measured values is a criterion of the precision of the present measurements.

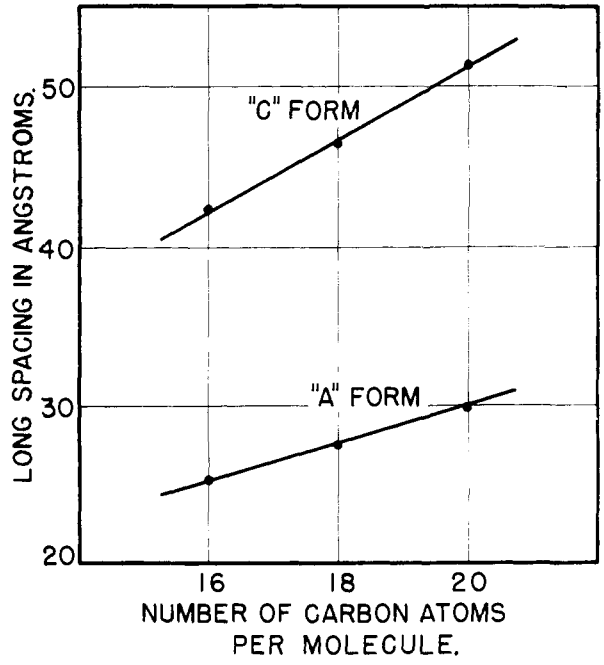

Fig. 1.—Relation between X-ray long spacings and number of carbon atoms in acetamide–fatty acid molecular compounds.

The third column of Table I, under the heading "A" Modification, gives the shorter of the spacings found for the addition compounds with myristic, palmitic and stearic acids. These spacings are shorter than those of any reported polymorphic form of the corresponding acids and indicate that the unit cell of this polymorphic modification of the acetamide compounds probably does not consist of the double-molecular length found for all saturated fatty acids.[8]

Assuming a unit cell only one molecule of acid and one molecule of acetamide in length, the long spacings for the molecular addition compounds can be calculated by adding to the known long spacings for the "A" forms of the three long-chain fatty acids, the long spacing for acetamide. From single-crystal measurements Senti and Harker[9] have reported the long *c*-axis for acetamide as 13.49 Å. For the "A" or untilted form of acetamide, *i.e.*, 90° angle of tilt, the X-ray long spacing will be identical to this crystallographic axis. The values in parentheses in the third column of Table I are one-half the sums of the most recently published values for the long spacings for the "A" forms of myristic, palmitic and stearic acids[7] and this value, 13.49 Å. for acetamide. Calculated and experimentally observed values show reasonably good agreement, confirming the fact that these spacings represent the "A" form of the molecular compounds.

In the fourth column of Table I, headed "C" Modification, the longer spacings of the acetamide compounds are given. The "C" forms of the fatty acids have an angle of tilt of 59° 12′.[10] The contribution of the acetamide molecule, if extended at this same angle of tilt, would be 13.49 sin 59° 12′, or 11.5 Å. Calculated values obtained by adding this value to the long spacing of the "C" forms of the corresponding acids[7] are given in parentheses in column 4 of Table I. These calculated spacings show reasonably good agreement with the experimental values and confirm the fact that these spacings represent the "C" form of the molecular adducts.

In Fig. 1 ("A" Form) the X-ray long spacings of the "A" form of the acetamide compounds are plotted against the number of carbon atoms per molecule for the three addition compounds. The solid line in this figure represents the best fit through the experimental points of a straight line with a slope of 1.26, *i.e.*, exactly one-half the slope of the non-tilted "A" form of the saturated fatty acids.[10] The agreement between experimental points and the solid line so constructed is satisfactory, the differences being not more than ±0.1 Å.

(5) F. C. Magne, R. R. Mod and E. L. Skau, *J. Am. Oil Chemists' Soc.*, **34**, 127 (1957).

(6) F. C. Magne and E. L. Skau, THIS JOURNAL, **74**, 2628 (1952).

(7) E. Stenhagen and E. v. Sydow, *Arkiv. Kemi*, **6**, No. 29, 309 (1953).

(8) A. Müller and G. Shearer, *J. Chem. Soc.*, **127**, 591 (1923); A. Müller, *Proc. Roy. Soc. (London)*, **A114**, 542 (1927).

(9) F. Senti and D. Harker, THIS JOURNAL, **62**, 2008 (1940).

(10) S. H. Piper, *Trans. Faraday Soc.*, **25**, 348 (1929).

TABLE I

X-RAY DIFFRACTION DATA

1	2	3			4			5
Fatty acids in acetamide addn. compd.	Free acid long spacing 2:0 Weak	"A" Modification of addn. compd. Long spacing 1:1 Strong	Short spacings		"C" Modification of addn. compd. Long spacing 2:2 Strong	Short spacings		"X" form of free acid long spacing 2:0 Weak
Lauric	27.4				18.6 [1:1]	9.32(M)	3.76(VS)	
	(27.4)				(19.4)	7.60(M)	3.32(MS)	
						6.60 (F)	2.95(M)	
						5.84(F)	2.73(F)	
						4.64(MS)	2.58(F)	
						4.21(VS)	2.52(F)	
						3.90(VS)	2.30(M)	
Myristic	31.6	25.3	9.10(M)	3.44(M)	42.4	8.01(M)	3.22(F)	37.0
	(31.7)	(25.1)	7.70(M)	3.23(F)	(43.1)	6.97(M)	3.01(F)	(36.7)
			5.93(M)	2.97(M)		6.01(F)	2.84(F)	
			4.56(F)	2.80(F)		5.30(F)	2.66(F)	
			4.07(VS)	2.68(F)		4.96(F)	2.55(F)	
			3.77(S)	2.41(M)		4.43(VS)	2.46(F)	
			3.62(M)	2.22(M)		4.12(VS)	2.41(F)	
			3.53(F)	2.15(F)		3.74(VS)	2.29(M)	
						3.58(S)	2.21(F)	
						3.41(F)		
Palmitic	35.7	27.6	9.17(M)	3.31(M)	46.5	7.18(F)	3.28(F)	
	(36.0)	(27.6)	7.95(M)	3.11(F)	(47.4)	4.45(M)	2.94(F)	
			5.95(M)	2.96(M)		4.12(VS)	2.47(F)	
			4.76(F)	2.72(F)		3.72(S)	2.21(F)	
			4.07(VS)	2.62(F)				
			3.76(S)	2.42(M)				
			3.63(F)	2.22(M)				
			3.49(M)	2.14(M)				
Stearic	39.8	29.9	8.19(M)	3.52(F)	51.4	8.10(F)	3.77(S)	
	(40.0)	(30.0)	6.98(M)	3.36(M)	(51.4)	7.40(F)	3.63(MS)	
			5.95(M)	2.97(M)		6.40(F)	3.49(F)	
			4.92(F)	2.87(F)		5.35(F)	3.34(F)	
			4.44(F)	2.64(F)		4.46(S)	2.42(F)	
			4.07(VS)	2.56(F)		4.26(F)	2.30(F)	
			3.91(F)	2.42(M)		4.06(S)	2.13(F)	
			3.76(S)	2.23(M)				
			3.64(F)	2.14(M)				

The fact that the experimental points fit a straight line proves that these "A" polymorphic modifications of the acetamide compounds with myristic, palmitic and stearic acids form an isomorphous series. The magnitude of the slope indicates a unit cell one molecule in length as reported for long-chain hydrocarbons, esters, etc.,[8] the slope being equal to the average increment of increase in long spacing per CH_2 group.

The experimental values for the long spacings of the "C" modifications of the acetamide compounds with myristic, palmitic and stearic acids are also plotted in Fig. 1 ("C" Form) against the number of carbon atoms per molecule for the three addition compounds. The solid line of this figure has been constructed as the best fit through these three experimental points with a line of exactly the slope, 2.25 Å.,[10] required for the "C" form of the parent fatty acids. The excellent agreement is somewhat fortuitous, considering that the experimental long spacings have been measured to only 0.1 Å. The straight line indicates that the "C" modification of the acetamide compounds with myristic, palmitic and stearic acids also forms an isomorphous series. The slope of this line indicates a unit cell length consisting of two molecules.[10] The average increment of increase in long spacing per CH_2 group calculated directly from the experimental data in Table I is 1.12 Å., in excellent agreement with the value of 1.10 given by Clark for the average increase in the homologous series of the "C" forms of the saturated fatty acids.[11]

The X-ray diffraction data for the lauric acid–acetamide adduct differ from those of the longer-chain homologs in several respects. First only one polymorphic form has been found. All attempts to prepare the "A" form have resulted in X-ray patterns identical to the "C" modification. The "C" form of this adduct has a spacing which corresponds to a calculated value based on a unit cell one molecule of lauric acid and one molecule of acetamide in length, in contrast to the "C" forms of the three homologs, which have a unit cell equal in length to two molecules of the fatty acid and two molecules of acetamide. Inspection of the X-ray patterns of numerous samples of the lauric acid–

(11) G. L. Clark, "Applied X-Rays," 4th Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1955.

acetamide compound indicates that there is no justification for doubling this spacing on the assumption that the first, and longest, reflection order has not been observed. Under identical conditions of measurement the longer first-order reflections of the myristic, palmitic and stearic acid addition compounds are observed. Furthermore, when the length of the first observed X-ray line in the pattern of the lauric acid–acetamide compound is doubled, only every other reflection order is obtained. Finally, the characteristic short spacings for the lauric acid adduct exhibit a somewhat different pattern from similar spacings for the "C" forms of the other adducts. The three strongest short spacings for the "C" forms of the addition compounds, for example

	I	II	III
Lauric	4.21	3.90	3.76
Myristic	4.43	4.12	3.74
Palmitic	4.45	4.12	3.72
Stearic	4.46	4.06	3.77

reveal the difference in the pattern of the lauric acid compound.

Under "X" in Table I is listed the long spacing for the myristic acid previously shown to agree with the value in parentheses reported by Slagle and Ott[3] for an unstable modification of this acid.

The fact that the two modifications of the fatty acid–acetamide compounds correspond to the "A" and "C" forms of the fatty acids suggested the possibility of preparing the "A" forms of the acids by dissolving the acetamide from the acetamide compound without melting. It was found, however, that when the acetamide was removed from the "A" form of the palmitic acid–acetamide compound by extraction with cold water, the X-ray diffraction pattern of the resulting product was that of the "C" form of the free palmitic acid.

There is a considerable difference between the short spacings listed in Table I for the two polymorphic forms of each of the molecular compounds. A combination of long and short spacings permits a ready and a positive identification of any of the addition compounds and of its polymorphic form.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Crystallography and Structure of Some C_{19} Cyclopropane Fatty Acids[1]

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RECEIVED MARCH 4, 1957

The unit cell dimensions and space groups have been determined for four synthetic fatty acids, *cis*- and *trans*-DL-9,10-methylene-octadecanoic and *cis*- and *trans*-DL-11,12-methylene-octadecanoic, and two natural products, lactobacillic acid and dihydrosterculic acid. The crystals of the two *cis* and two *trans* synthetic acids, respectively, are isomorphous for reasons apparent from the packing shape of the molecules. The crystal structure of the dihydrosterculic acid is identical with that of the *cis*-DL-9,10 synthetic acid. The lactobacillic acid crystal structure is different from that of any of the synthetic products. The crystal data in combination with chemical evidence point to the *cis*-D- or L-11,12-methylene-octadecanoic acid structure for lactobacillic acid. From powder diffraction data the acid amides are shown to have similar crystal structural relationships.

The Crystallography of the C_{19} Cyclopropane Acids.—Six $C_{19}H_{36}O_2$ cyclopropane fatty acids are known from the work of Hofmann and his collaborators[2-5]; the *cis*- and *trans*-DL-9,10-methylene-octadecanoic acids and the *cis*- and *trans*-DL-11,12-methylene-octadecanoic acids, which were prepared synthetically; the lactobacillic and dihydrosterculic acids, which were obtained from natural products.[6]

The crystal habit of these acids is similar to that of the normal long-chain fatty acids. Single crystals are difficult to obtain and always appear in thin plates on (001), with the conventional assignment of the long axis as *c*. The so-called "pseudo single crystals"[7] are commonly obtained from a variety of solvents and mixed solvents. In this form of crystal imperfection, multiple thin platy crystals are aligned with one axis in common and the other more or less regularly disordered, like the pages of a book. Even crystals which appeared to be true single crystals under the microscope nearly always showed evidence of this type of imperfection to a more or lesser degree on the X-ray photographs. Conspicuously, the natural products were more difficult to crystallize than the synthetic compounds and gave poorer powder diffraction patterns. The single crystals used in this research were obtained by recrystallization from 5:1 acetone–water mixture at 0°.

The crystallographic data on these acids are given in Table I, together with those of some normal and branched-chain fatty acids of comparable chain length. The values of a, b, α, γ, and c sin β (the long spacing) are measured directly from the X-ray photographs. The selection of the values for β is arbitrary and it is convenient to choose β so that it corresponds to the projection on (010)

(1) Work done jointly in the Sarah Mellon Scaife Radiation Laboratory and the Chemistry Department and supported by a research grant from the Department of Health, Education and Welfare, Public Health Service, National Institutes of Health.

(2) K. Hofmann and R. A. Lucas, THIS JOURNAL, **72**, 4328 (1950).

(3) K. Hofmann, R. A. Lucas and S. M. Sax, *J. Biol. Chem.*, **195**, 473 (1952).

(4) K. Hofmann, O. Jucker, W. R. Miller, A. C. Young, Jr., and P. Tausig, THIS JOURNAL, **76**, 1799 (1954).

(5) K. Hofmann, S. F. Orochena and C. W. Yoho, *ibid.*, **79**, 3608 (1957).

(6) The specimens used in this research were provided by Dr. K. Hofmann, Biochemistry Department, University of Pittsburgh.

(7) A. Muller, *Proc. Roy. Soc.* (*London*), **A114**, 542 (1927).