The X-Ray Diffraction of Molecular Compounds of 2-Aminopyridine with Long Chain Saturated and Unsaturated Fatty Acids

EVALD L. SKAU, ROBERT R. MOD, FRANK C. MAGNE, and ROBERT T. O'CONNOR
Southern Regional Research Laboratory[1], New Orleans, Louisiana 70179

ABSTRACT

X-Ray diffraction measurements of long and short spacings are reported for the crystalline 1:1 and 4:1 molecular compounds of 2-aminopyridine with the C_{10} to C_{18} saturated fatty acids and the 1:1 and 2:1 compounds of oleic, elaidic, alpha-eleostearic and beta-eleostearic acids. Data are also reported for 2-aminopyridine, α-eleostearic acid and β-eleostearic acid. The angle of tilt of the 1:1 saturated compounds is 42°15′. The long spacings of the 4:1 compounds indicate a unit cell length of four molecules of fatty acid and one molecule of 2-aminopyridine with an angle of tilt of 62°15′. The contribution of the 2-aminopyridine to the length of a molecule of the 1:1 compounds is ca. 6 Å, the distance between the NH_2 and the CH_2 in the para position. In the 4:1 and 2:1 compounds it is ca. 3 Å, the distance between the NH_2 and the ring nitrogen.

INTRODUCTION

In their investigations of molecular compounds of long chain fatty acids, Mod and Skau (1) have reported binary freezing point data for 2-aminopyridine with saturated and unsaturated long chain fatty acids which prove the existence of two congruently melting, crystalline, molecular compounds in each case. In this paper, X-ray diffraction data on these molecular compounds are reported, and the results discussed in connection with proposed structure.

EXPERIMENTAL PROCEDURES

The molecular compounds of 2-aminopyridine with capric, lauric, myristic, palmitic, stearic and elaidic acids were prepared by solvent crystallization of the appropriate amine-acid mixture (2). The unsaturated oleic, and α- and β-eleostearic acid compounds were made by fusing the proper proportions of the pure acid and amine in a sealed tube. For saturated acid systems, the compounds have the compositions $NC_5H_4NH_2 \cdot RCOOH$ and $NC_5H_4NH_2 \cdot 4RCOOH$ and for the unsaturated systems, $NC_5H_4NH_2 \cdot RCOOH$ and $NC_5H_4NH_2 \cdot 2RCOOH$. All melting points were the same as previously reported (1,2) for the pure compounds.

The X-ray measurements were made by the powder method as described in earlier papers (3,4).

One set of long spacings has been found for each of the 1:1 compounds, and two long spacings were observed for each of the 4:1 compounds. The 4:1 compound of capric acid was not investigated. All of the reported long spacings in Table I are averages of several orders of diffraction from measurements on two or more independently prepared diffraction patterns. The second set of long spacings observed in the case of the 4:1 addition compounds agrees very well (within an average of 0.3 Å) with the latest accepted values for the spacings of the "C" form of the free long chain saturated acids (5) (Table I, in parentheses in column 8).

[1]S. Market. Nutr. Res. Div., ARS, USDA.

The experimental values for the long spacings, L, of the five 1:1 compounds when plotted against the number of carbon atoms, n, in the fatty acid molecule, give a straight line, proving that the compounds form an isomorphous series. The same is true of the 4:1 compounds. Least squares calculations for the 1:1 compounds give the linear equation $L=0.854n + 6.50$, showing that d_{obs}, the average increase in observed long spacing per carbon atom, is 0.854 Å. The average and maximum deviations of the individual experimental values from this equation are 0.03 and 0.04 Å, respectively.

The angle of tilt, Θ, equals arc sin (d_{obs}/d_{90}) where d_{90} is the average increment of long spacing per carbon atom which would be observed if there were no tilt, i.e., if Θ were 90°. Since d_{90} is 1.27 Å (6), the angle of tilt of the 1:1 compounds is 42°15′. This is very close to the value reported for the neutral ammonium salts, 45°40′ (7). The corresponding calculations for the 4:1 compounds give the equation $L=4.494n + 11.04$; average deviation, 0.05 Å; maximum deviation, 0.12 Å; angle of tilt, arc sin (1.124/1.27) or 62°15′.

The magnitude of the long spacing for the 1:1 compounds shows that the probable length of the unit cell is equal to the sum of the lengths of one molecule of fatty acid and one molecule of 2-aminopyridine. The length contibuted to the long spacing by the fatty acid (Table II, column 2) can be estimated by multiplying the length $L_{90}/2$ by the sine of the angle of tilt, sin 42°15′. L_{90} is the long spacing which would be obtained for the fatty acid (double molecules) if the long chains were perpendicular to the reflecting planes. It can be calculated from the equation $L_{90}=2.538n + 5.12$, where n is the number of carbon atoms per acid molecule (Reference 6, Table I).

The difference between the observed long spacing for the 1:1 compound (Table I, column 2) and the contribution of the fatty acid portion at the 42°15′ angle of tilt (Table II, column 2) gives the contribution of the 2-aminopyridine portion to the observed long spacing, 4.8 Å (column 3).

As not crystallographic data appear to be available for 2-aminopyridine, diffraction patterns for this compound were measured (Table III). The "long spacing," 11.99 Å, is the average of four orders from three independently measured diffraction patterns. Assuming two molecules per unit cell and a 90° angle of tilt, the length of the molecule would be 6.00 Å. This is in good agreement with the maximum length of the 2-aminopyridine molecule, 5.5-6.2 Å, the distance from the amine group to the CH_2 in para position in the ring calculated from data on atomic distances and valence bond angles (8).

If the long axis of the 2-aminopyridine moiety is considered as a linear extension of the long chain fatty acid, i.e., at the same angle of tilt, 42°15′, its contribution to the observed long spacing of the 1:1 compound would be 6.0 sin 42°15′ or 4.1 Å. This is in reasonable agreement with the value of 4.8 Å, the observed contribution shown in Table II, column 3.

Less satisfactory agreement is obtained when the same treatment is applied to the data for the 4:1 compounds. The magnitude of the long spacings and the molecular composi-

TABLE I

X-Ray Data for Molecular Compounds of 2-Aminopyridine with Saturated Long Chain Fatty Acids, Å

Fatty acid	1:1 Molecular compound		4:1 Molecular compound		Free acid (C form) long spacing
	Long spacing	Short spacings[a]	Long spacing	Short spacings[a]	
Capric	15.07	7.52MS 3.74S 5.58MS 3.50M 5.26M 3.40F 4.93M 3.22F 4.69M 2.97M 4.48M 2.70F 4.25F 2.55F 4.12M 2.41F 3.97F 2.14F			
Lauric	16.72	9.40M 3.96MS 8.44MS 3.83M 5.62M 3.63MS 5.34MS 3.42M 5.00F 3.18M 4.67MS 2.77F 4.50MS 2.40F 4.32MS 2.03F	64.94	4.78MS 3.00F 4.40M 2.53F 4.17MS 3.89S 3.59F 3.42F 3.30F	27.18 (27.4)
Myristic	18.46	9.44S 3.87S 5.58MS 3.72MS 5.12F 3.58M 4.67M 3.36M 4.55M 3.16F 4.39M 2.95F 4.18M 2.62F 4.06M 2.40F	74.02	4.79MS 3.00F 4.59F 2.81F 4.39MS 2.63F 4.19S 2.52F 3.93S 2.38F 3.81S 2.32F 3.45M 2.26F 3.33F 2.14F 3.22F	31.33 (31.7)
Palmitic	20.12	10.18S 4.05MS 6.75F 3.77S 5.62M 3.62M 5.19M 3.51M 4.63MS 3.11M 4.43MS 2.77F 4.26F 2.34F	82.90	4.77MS 3.43F 4.55F 3.35F 4.38MS 3.22F 4.18S 3.14F 4.07M 2.97F 3.95MS 2.50F 3.83S 2.37F	35.52 (36.0)
Stearic	21.91	11.10M 3.94S 8.91F 3.83M 7.35F 3.68S 5.46M 3.26M 5.01M 2.93M 4.63M 2.72F 4.47S 2.64F 4.32M 2.50F 4.19F 2.39FF 4.05F 2.15FF	91.94	4.74M 3.09F 4.55M 2.96F 4.37M 2.51F 4.14S 2.38F 3.92M 2.30F 3.79MS 3.51F 3.29F	39.71 (40.0)

[a]VS, very strong; S, strong; MS, medium strong; M, medium; F, faint; VF, very faint; Br, broad.

tion of the 4:1 compounds indicate that the repeating unit of the crystal lattice involves one 2-aminopyridine molecule attached to four fatty acid molecules, the latter being arranged linearly end-to-end or end-to-tail, as, for example: $NC_5H_4NH_2 \cdot HOOCR \cdot RCOOH \cdot HOOCR \cdot RCOOH$. The approximate length contributed by the fatty acid portion (Table II, column 4) can be estimated by multiplying the length $2L_{90}$ by the sine of 62°15′, the angle of tilt. The deviation of the resulting value from the observed long spacings for the 4:1 compounds (Table I, column 5) gives the contribution of the 2-aminopyridine portion to the observed long spacings, 2.1 Å (Table II, column 5). Considering the long axis of the 2-aminopyridine moiety as a linear extension of the long chain of the fatty acid, its contribution to the observed long spacing of the 4:1 compound would be 6.0 sin 62°15′ or 5.1 Å instead of 2.1 Å.

This 3 Å difference can be explained by the fact that in the 4:1 compounds both the NH_2 and the ring nitrogen are undoubtedly hydrogen bonded to carboxyl groups. Thus instead of a contribution of 6 Å to the cell length, i.e., the distance from the NH_2 to the para position in the pyridine ring, the much shorter distance, ca. 3 Å, between the NH_2 and the ring nitrogen is involved.

TABLE II

Contribution of Saturated Acids and 2-Aminopyridine to the Long Spacings of Their Molecular Compounds, Å

n	1:1 Compounds Contribution by		4:1 Compounds Contribution by	
	Acid	Amine	Acid	Amine
10	10.25	4.82		
12	11.96	4.76	62.98	2.16
14	13.67	4.79	71.96	2.06
16	15.37	4.75	80.95	2.01
18	17.08	4.83	89.79	2.15

SHORT SPACINGS

The strongest short spacings are very similar for the various members of a homologous series of the molecular compounds. For the five 1:1 compounds the strongest

TABLE III

X-Ray Diffraction Data in Angstroms

Compound	Long spacing	Short spacings
2-Aminopyridine	11.99	5.86 M, 4.56 S, 4.32 M, 4.16 M, 4.07 F, 3.79 M, 3.71 S, 3.51 M, 3.15 M, 3.10 S, 2.59 F, 2.52 F, 2.39 F, 2.30 F, 2.20 F, 2.03 F, 1.88 F, 1.84 F, 1.80 F
α-Eleostearic acid	40.5	4.61 S, 4.40 MS, 4.09 VS (Broad), 3.84 MS, 3.61 M, 3.32 F, 3.13 M, 3.03 M, 2.95 F, 2.30 F, 2.24 M
β-Eleostearic acid	47.7	4.08 VS, 3.67 M, 3.55 F, 3.41 F, 3.26 F, 3.04 F, 2.92 F, 2.72 F, 2.49 F, 2.20 F

short spacing is found at ca. 3.7 Å, the second strongest at ca. 4.5 Å and the third strongest at ca. 5.6 Å. The four members representing the 4:1 compounds exhibit three strongest short spacings at about 3.9, 4.2 and 4.8 Å. From a combination of the long spacing and the three strongest short spacings any member of either homologous series can be uniquely identified.

MOLECULAR COMPOUNDS WITH UNSATURATED LONG CHAIN ACIDS

X-Ray diffraction data obtained for both the 1:1 and 2:1 molecular compounds of 2-aminopyridine with the unsaturated long chain fatty acids oleic, elaidic, α-eleostearic and β-eleostearic, are given in Table IV. The long spacings for the compounds with oleic and with α-eleostearic acids were obtained at reduced temperatures (-5 to +5 C), and no measurements were made of the short spacings.

Lutton (9) has shown that oleic acid crystallizes in two modifications, a lower-melting form with a long spacing of 40.5 Å and a higher-melting form with a long spacing of 84.4 Å, or possibly 42.2 Å. The spacing for a single molecule would be ca. 20-21 Å, nearly the same as the observed long spacing for the 1:1 compound with 2-aminopyridine, 21.36 Å. This can only mean that the fatty acid portion of the 1:1 compound has a considerably greater tilt (a lower angle of tilt), with respect to the reflecting planes, than that of the free oleic acid.

Five values have been reported for the long spacing of the common form of elaidic acid (10-14), all agreeing rather well with the average of 48.92 Å for a unit cell with two molecules of elaidic acid. (The value 47.0 Å was reported (14) for the long spacing of a new polymorphic modification) Here the value for a single molecule, either 24.46 or 23.5 Å, would be greater than the observed long spacing for the 1:1 compound with 2-aminopyridine, 21.90 Å. It must therefore be concluded that for elaidic acid, the tilt of the fatty acid molecule in the 1:1 compound is much greater than in either modification of the crystalline acid, the difference being considerably greater than the corresponding difference for the oleic acid compound.

No X-ray diffraction data for pure α- and β-eleostearic acids appear to be available in the literature. Measurements made in this Laboratory are reported in Table III. The sum of the long spacing for the pure crystalline α-eleostearic acid, 20.25 Å per molecule, and the maximum increment for one molecule of 2-aminopyridine, 6 Å, is very close to

TABLE IV

X-Ray Data for Molecular Compounds of 2-Aminopyridine with Unsaturated Long Chain Fatty Acids in Angstroms

	1:1 Compound			2:1 Compound		
Fatty acid	Long spacing	Short spacings		Long spacing	Short spacings	
Oleic	21.36			35.41		
Elaidic	21.90	11.16MS	4.18F	52.25	9.49M	3.57F
		8.95F	3.96S		8.49F	3.43M
		7.42M	3.84S		6.49M	3.24M
		5.65M	3.69S		5.58M	3.05F
		5.46MS	3.45F		5.06F	2.95F
		5.02M	3.24M		4.75S	2.85F
		4.60M	2.93M		4.54S	2.77F
		4.47S	2.65F		4.39F	2.69F
		4.32MS	2.49F		4.14VS	2.43M(Br)
			2.40F		3.98S	2.30F
			2.31F		3.86MS	2.18F
			2.16F		3.75VS	2.12F
α-Eleostearic	26.51			35.57		
β-Eleostearic	25.28	8.50M	3.18M	26.84	9.21M	3.49MS
		7.09F	3.02F	(53.72)	7.40M	3.32M
		6.32F	2.88F		6.45F	3.19MS
		5.18VS	2.73F		5.87F	3.10F
		4.77MS	2.64F		5.40F	3.01F
		4.32VS	2.52F		5.04MS	2.92M
		4.11F	2.41F		4.71M	2.70F
		3.93VS	2.31F		4.45M	2.58F
		3.72VS	2.11F		4.18VS	2.50MS
		3.52VS	1.89F		4.07VS	2.35F
		3.28M			3.91F	2.23F
					3.79MS	2.06F
					3.66MS	1.98F

the observed value for the long spacing of the 1:1 compound, 26.51 Å. It follows that the tilt of the fatty acid portion of the 1:1 compound must be equal to or less than that in the pure crystalline acid. By similar reasoning, it appears from the long spacing of the pure crystalline β-eleostearic acid, 23.85 Å per molecule, and that of the 1:1 compound, 25.28 Å, that the tilt of the β-eleostearic acid portion of the 1:1 compound is probably somewhat greater that that found for the crystalline acid.

The contribution of the 2-aminopyridine to the length of the molecules of the 2:1 compounds would be ca. 3 Å, since here again the carboxyls would be bonded to both the NH_2 and the ring nitrogen. The long spacings for oleic and α-eleostearic acids (double molecules) are much greater than those for their 2:1 compounds. It follows that the tilt of the acid portion of the 2:1 crystals is greater than in the parent acid. The data for the 2:1 elaidic acid compound are insufficient to draw definite conclusions in this respect.

The 2:1 compound with β-eleostearic acid exhibits the longest long spacng of 26.84 Å. This spacing is much too short to account for the length of two molecules of the β-eleostearic acid plus one molecule of 2-aminopyridine. If, however, this spacing is considered the second order of diffraction, we arrive at an average spacing, based upon 13 of the first 17 orders, of 53.72 Å, a more reasonable value for the long spacing of this compound. This value is, however, now greater than the combined spacing of the free β-eleostearic acid, 47.7 Å and the 3 Å assigned to the 2-aminopyridine moiety. This would imply that the tilt of the fatty acid portion of the 2:1 compound is considerably less than that in the crystalline free acid.

REFERENCES

1. Mod, R.R., and E.L. Skau, J. Phys. Chem. 60:963 (1956).
2. Mod, R.R., F.C. Magne and E.L. Skau, JAOCS 36:616 (1959).
3. O'Connor, R.T., R.R. Mod, M.D. Murray and E.L. Skau, J. Am. Chem. Soc. 77:892 (1955).
4. O'Connor, R.T., R.R. Mod, M.D. Murray, F.C. Magne and E.L. Skau, Ibid. 79:5129 (1957).
5. Stenhagen, E., and E. von Sydow, Ark. Kemi 6:309 (1953).
6. Skau, E.L., JAOCS, in press.
7. Vand, V., W.M. Morley and T.R. Lomer, Acta Cryst. 4:324 (1951).
8. Wheland, G.W., "Resonance in Organic Chemistry," John Wiley & Sons, Inc., New York, 1955.
9. Lutton, E.S., Oil Soap 23:265 (1946).
10. Müller, A., and G. Shearer, J. Chem. Soc. 123:3156 (1923).
11. Benedict, J.H., and B.F. Daubert, J. Am. Chem. Soc. 71:4113 (1949).
12. Lutton, E.S., and D.G. Kolp, Ibid. 73:2733 (1951).
13. Swern, D., L.P. Witnauer, S.A. Fusari and J.B. Brown, JAOCS 32:539 (1955).
14. Harris, J.A., R.R. Mod and E.L. Skau, Ibid. 44:737 (1967).

[Received May 25, 1972]