taken up in 15 ml. of ethanol, treated with charcoal, filtered, diluted with water until barely cloudy at 40°, reheated and allowed to cool. The yield of white needles was 0.45 g. Another crystallization from ethanol–water gave material melting at 93°.

Anal. Calcd. for $C_{17}H_{15}NOS$: C, 72.56; H, 5.37; N, 4.98. Found: C, 72.73; H, 5.49; N, 5.04.

1-Methyl-3,4-dihydrothianaphtheno(2,3-*C*)pyridine.—One and two-tenths grams of V was refluxed with 2.4 g. of phosphorus pentoxide and 2.4 g. of phosphorus oxychloride in anhydrous xylene for one hour. The cold mixture was decomposed with ice. The aqueous layer was separated, washed with benzene, made basic with concentrated sodium hydroxide solution and extracted with three 25-ml. portions of benzene. The combined benzene extracts were dried over sodium sulfate and concentrated at reduced pressure. The residual red sirup solidified on stirring with a little petroleum ether and was taken up in 100 ml. of that solvent. The solution was decolorized with charcoal, filtered and concentrated to 15 ml. on chilling; 0.6 g. of white product separated. Another recrystallization gave crystals melting at 73.5°, soluble in dilute acid with yellow color, insoluble in base.

Anal. Calcd. for $C_{12}H_{11}NS$: C, 71.59; H, 5.51; N, 6.96. Found: C, 71.66; H, 5.54; N, 6.86.

Addition of picric acid solution to a solution of the product in ethanol immediately precipitated the picrate. After recrystallization from a large volume of ethanol it decomposed at 227–228° when the capillary was immersed at a temperature of 220°.

Anal. Calcd. for $C_{18}H_{14}N_4O_7S$: N, 13.02. Found: N, 12.61.

1-Phenyl-3,4-dihydrothianaphtheno(2,3-*C*)pyridine.—Cyclization of 1 g. of the benzoyl derivative in the same manner yielded 0.65 g. of crude product. The white needles melted at 64° after recrystallization from petroleum ether.

Anal. Calcd. for $C_{17}H_{13}NS$: C, 77.54; H, 4.98; N, 5.32. Found: C, 77.70; H, 4.79; N, 5.35.

The picrate decomposed at 196–198°.

Anal. Calcd. for $C_{23}H_{16}N_4O_7S$: N, 11.37. Found: N, 1.02.

1-Methylthianaphtheno(2,3-*C*)pyridine.—One gram of the dihydro compound was heated with 1 g. of palladium black in a small test-tube at 190–200° for thirty minutes. The cold mixture was extracted thoroughly with acetone, the acetone was treated with charcoal, filtered and evaporated to dryness at reduced pressure. The residue was taken up in 50 ml. of low-boiling petroleum ether, decolorized with charcoal and concentrated to 5 ml. On chilling, 0.4 g. of white crystals, m. p. 109°, was obtained. Sublimation at 100° (0.5 mm.) yielded a product melting at 110°.

Anal. Calcd. for $C_{12}H_{9}NS$: C, 72.32; H, 4.56; N, 7.03. Found: C, 72.65; H, 4.51; N, 6.82.

The picrate, recrystallized from a large volume of ethanol, decomposed at 262°.

Anal. Calcd. for $C_{18}H_{12}N_4O_7S$: N, 13.08. Found: N, 12.89.

1-Phenylthianaphtheno(2,3-*C*)pyridine.—Dehydrogenation of 1.35 g. of VIII was carried out in the manner described above. The acetone extract was treated with charcoal and concentrated to 15 ml. On cooling 0.52 g. of slightly-colored crystals separated. Concentration of the filtrate to 5 ml. and addition of a few drops of water yielded an additional 0.21 g. The product melted at 152.5° after recrystallization from acetone.

Anal. Calcd. for $C_{17}H_{11}NS$: C, 78.09; H, 4.24; N, 5.37. Found: C, 78.41; H, 4.33; N, 5.41.

The picrate was recrystallized from ethanol, m. p. 208–209° (dec.).

Anal. Calcd. for $C_{23}H_{14}N_4O_7S$: N, 11.38. Found: N, 11.73.

Summary

The synthesis of 1-methyl- and 1-phenylthianaphtheno(2,3-*C*)pyridine is reported. The former is the sulfur analog of harman.

TALLAHASSEE, FLORIDA RECEIVED APRIL 28, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY AND NUTRITION, TEXAS AGRICULTURAL EXPERIMENT STATION, TEXAS AGRICULTURAL AND MECHANICAL COLLEGE SYSTEM, COLLEGE STATION]

Separation and Stabilization of Fatty Acids by Urea Complexes[1]

BY HERMAN SCHLENK AND RALPH T. HOLMAN

After Bengen[2] had discovered the phenomenon of urea complex formation with normal aliphatic compounds in 1940, further research was carried on in the Oppau laboratory of the former I. G. Farbenindustrie A. G. The results of their detailed investigations of the structure and formation of the complexes, steric limitations, and energy relationships appeared in 1949.[3,4] Since the release of the Technical Oil Mission reports,[5] considerable interest has been aroused in this country. Attention was called to urea complexes by the group at Standard Oil Laboratories in 1949.[6,7] Recently the principal results of Schlenk were confirmed[8,9] and separations based upon urea complexes have been achieved in pilot plant scale.[10]

The earlier reports indicated that normal compounds could be separated from branched compounds. Such separations are based upon differences in molecular shape, and it seemed likely that unsaturation might cause sufficient change in the shape of normal compounds to

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(1) Supported in part by a contract between the Office of Naval Research and the Texas A. and M. Research Foundation. Presented at the 117th A. C. S. meeting, Houston, Texas, March, 1950.

(2) F. Bengen, German patent application (March 18, 1940).

(3) F. Bengen and W. Schlenk, Jr., *Experientia*, **5**, 200 (1949).

(4) W. Schlenk, Jr., *Annalen*, **565**, 204 (1949).

(5) Technical Oil Mission Reel 6, frames 263–270 in German, Reel 143, pages 185–189 in English (Copies and translations of ref. 2).

(6) W. J. Zimmerschied, R. A. Dinerstein, A. W. Weitkamp and R. F. Marschner, THIS JOURNAL, **71**, 2947 (1949).

(7) W. J. Zimmerschied, R. A. Dinerstein, A. W. Weitkamp and R. Marschner, *Ind. Eng. Chem.*, **42**, 1300 (1950).

(8) O. Redlich, C. M. Gable, A. K. Dunlop and R. W. Millar, THIS JOURNAL, **72**, 4153 (1950).

(9) H. A. Newey, E. C. Shokal, A. C. Mueller, T. F. Bradley and L. C. Fetterly, Abst. 117th ACS Meeting, Detroit, April 1950, p. 5-M.

(10) W. A. Bailey, Jr., R. A. Bannerot, L. C. Fetterly and A. G. Smith, Abst. 117th ACS Meeting, Houston, March 1950, p. 12-N.

permit separation of saturated and unsaturated substances. Therefore, the urea complexes of a series of saturated and unsaturated fatty acids were prepared and studied.

Preparations and Results

The fatty acids of the saturated series used in these investigations were found to be chromatographically homogeneous by single displacements.[11] The unsaturated fatty acids had the following chemical or physical constants: oleic acid iodine value 85; elaidic acid m. p. 44°; petroselinic acid m. p. 29°; petroselaidic acid m. p. 51–53°; linoleic acid I. V. 178; 10,12-linoleic acid m. p. 55°; linolenic acid I. V. 266; α-eleostearic acid m. p. 44°; β-eleostearic acid m. p. 69°; *pseudo*-eleostearic acid m. p. 77°; erucic acid m. p. 32°; and brassidic acid m. p. 57°.

TABLE I

YIELD AND COMPOSITION OF FATTY ACIDS UREA COMPLEXES

Acid	Yield, g. complex/g. acid	Composition, moles urea/mole acid
Caprylic	0.09	7.6
Capric	0.3	9.6
Lauric	0.9	10.3
Myristic	2.2	11.8
Palmitic	3.2	12.6
Stearic	3.3	14.3
Arachidic	3.6	16.0
Behenic (+$CHCl_3$)	3.9	16.7
Oleic	1.05	13.7
Elaidic	1.4	14.2
Petroselinic	1.7	..
Petroselaidic	3.4	14.1
Linoleic	0	13.1
10,12-Linoleic	2.7	14.2
Linolenic	0	13.6
α-Eleostearic	1.45	13.7
β-Eleostearic	1.4	14.0
pseudo-Eleostearic	2.2	13.7
Erucic	3.1	16.8
Brassidic	3.6	16.8

TABLE II

SEPARATION OF BINARY MIXTURES OF FATTY ACIDS

	Components	Urea, g.	Methanol, ml.	Complex fraction	Soluble fraction
A	9.9 g. lauric acid 9.9 g. stearic acid	30	150	10.5 g. 88% stearic acid	8.3 g. 83% lauric acid
B	2.4 g. lauric acid 2.4 g. linoleic acid	11.7	72	1.33 g. 73% lauric acid	
C	3.0 g. oleic acid 3.0 g. stearic acid	19.3	120	3.3 g. 80% stearic acid	2.65 g. 89% oleic acid
D	2.0 g. linoleic acid 2.0 g. stearic acid	9.6	60	1.9 g. 95% stearic acid	2.0 g. 79% linoleic acid
E	1.0 g. oleic acid 1.0 g. linoleic acid	4.8	30	0.6 g. 91.8% oleic acid	1.3 g. 57% linoleic acid
F	2.6 g. linoleic acid 2.6 g. linolenic acid	13	79	1.4 g. 80% linoleic acid	
G	1.0 g. stearic acid 1.0 g. β-eleostearic acid	4.8	30	0.96 g. 86% stearic acid	1.0 g. 76% eleostearic
H	0.89 g. oleic acid 0.89 g. β-eleostearic acid	4.8	30	0.76 g. 55% β-eleostearic	1.0 g. 62% oleic acid

All these unsaturated fatty acids were prepared by the accepted procedures. The complexes of the series of pure fatty acids were prepared in the following empirical manner. One gram of fatty acid was dissolved by warming in 30 ml. methanol which had been saturated with urea at room temperature (about 16 g./100 ml.). Upon cooling to room temperature (25°), the mixtures deposited crystalline urea complexes which were filtered off and dried. For the study of the tendencies of the various acids to form complexes, the weights of these crude crystalline preparations were taken as yields. The crude material was pure enough for such comparisons. For determination of the composition of the complexes, they were recrystallized from isopropyl alcohol until the acid values were constant. Slight variations in procedure were necessary to obtain complexes from some acids. For example, behenic acid could be brought to form complex best by increasing its solubility by adding a little chloroform, and some unsaturated acids did not precipitate as a complex until the temperature was lowered below room temperature. However, decreasing the temperature too far or too rapidly often caused the precipitation of urea mixed with the complex.

In Table I are summarized the yields of the complexes of the various acids under the standardized conditions and the composition of the recrystallized complexes. It will be seen that the chain length of the fatty acids regulates the composition of the complexes. This is in agreement with the results of previous work.[4] However, the composition of the unsaturated fatty acid complexes is not greatly different from that of the corresponding saturated compounds.

It is apparent from Table I that several factors influence these yields of complexes from the fatty acids. In the saturated series, the longer the chain, the higher the yield. Within the unsaturated non-conjugated acids, increasing unsaturation decreases the yield. Conjugated isomers give higher yields of complex than do non-conjugated isomers. *trans*-Mono-unsaturated acids give slightly higher yields than do their *cis* isomers. These differences in yields of complexes from the various fatty acids suggested that the various types of acids could be fractionated by means of urea complexes, and that prediction could b made which components of a mixture should first form a solid complex. These conclusions were tested by fractionation of a series of model mixtures.

The results of these attempted separations are summarized in Table II. The degree of separation of the components in the model mixtures is in good agreement with the differences in yield of complex from the individual acids. When the difference in yields is high for a pair of acids, fractionation is very effective. On the other hand,

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[11] L. Hagdahl and R. T. Holman, THIS JOURNAL, **72**, 701 (1950).

separation is poor when the yields are nearly equal, as in the case of oleic acid and β-eleostearic acid.

It is apparent that in the saturated series, the regular changes in solubility and melting point of the acids are reflected in the regular changes in properties of the complexes. For example, yields increase with increasing melting point and decreasing solubility. Such results, however, do not hold outside of a homologous series. It is especially interesting to point out that although stearic acid and β-eleostearic acid have melting points of 69 and 71°, respectively, they give widely different yields of complex and are easily separable. On the other hand, β-eleostearic acid and oleic acid (m. p. 13°) give nearly identical yields of complex and separation by urea complexes is inefficient. The solubilities of stearic and β-eleostearic acids in methanol at 25° are approximately 1.0 and 4.0 g./100 ml., respectively, but oleic acid is miscible with methanol in all proportions at 25°. Reasoning from differences in solubility of the acids themselves, oleic and β-eleostearic acids should be more easily separable than stearic and β-eleostearic acids. However, the inverse is true. This example points out that prediction of separabilities cannot be made from the melting points and solubilities, but that the detailed structure of the fatty acids must be considered also.

Applying these findings to natural products, it has been found possible to enrich the saturated and unsaturated acids from natural oils. The complexes of the acids in natural mixtures were prepared by heating the acids with urea in the presence of methanol. After cooling, the liquid was removed from the complexes either by decanting, filtration, or by pressing with a hydraulic press. The acids (or esters) were recovered from the complexes by warming the complex with ten times its weight of dilute hydrochloric acid. The acids were extracted with petroleum ether and dried before analysis.

From the results shown in Table III and from previously reported experiments,[12] it is clear that enrichments of the saturated and unsaturated acids are easily achieved in a wide variety of mixtures. The complex fraction contains an enrichment of saturated acids and the non-complex fraction contains an enrichment of unsaturated acids. By the proper selection of proportion of urea used, the composition of the two fractions can be varied according to will. The results in segregation of the acids from natural mixtures were encouraging enough to warrant attempts at preparation of pure unsaturated acids or esters by urea fractionation.

TABLE III

ENRICHMENTS OF NATURAL MIXTURES OF FATTY ACIDS

Fatty acids of	I. V.	Urea, g.	Methanol, ml.	Complex fraction g.	Complex fraction I. V.	Non-complex fraction g.	Non-complex fraction I. V.
Chinese tallow, 51 g.	19	100	150	27	6.5	18.5	38
Olive oil, 50 g.	81	50	150	13	46	37.7	85.5
Corn oil, 50 g.	126.5	75	150	21	81	26	164
Gourd seed oil, 49 g.	148	50	100	14.7	81	34	160
Soybean oil, 50 g.	141	100	100	33.5	119	13.7	191
Linseed oil, 50 g.	169	75	150	20	109	29	204

In the preparation of pure unsaturated substances it was desirable to use methyl esters to permit fractional distillation as a purification step. For the preparation of methyl oleate (see Fig. 1) minimal quantities of solvent were used and collection of the complexes was done with the hydraulic press. The experiment was planned to remove first two successive 10% portions of the olive oil methyl esters to eliminate saturated acids. The main portion of the esters (oleate) was then precipitated as complex, leaving the bulk of the linoleate in the liquid phase. The esters recovered from this complex fraction were fractionated by distillation and the C_{18} fraction was then predominantly methyl oleate with methyl linoleate as a contaminant. The oleate was then preferentially precipitated as complex leaving the linoleate in solution. The methyl oleate thus obtained in complex form was found to contain 2.2% methyl linoleate by alkaline isomerization.[13] Calculation from iodine value indicates 3.2% linoleate. Thus, stearic acid cannot be present in more than traces.

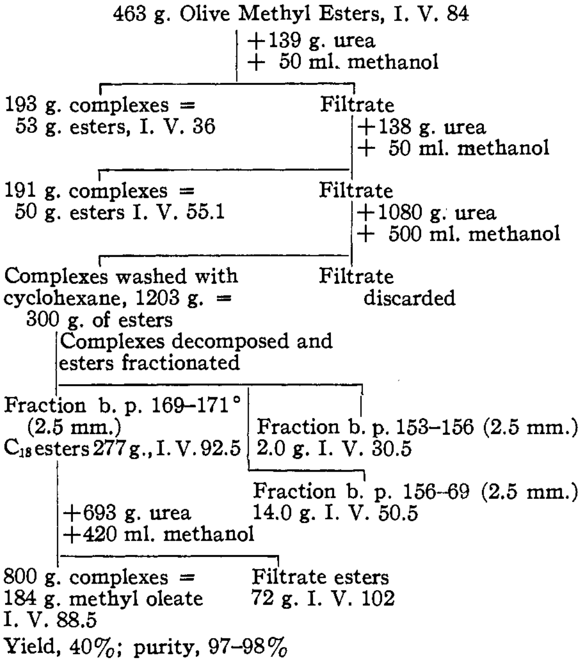

Fig. 1.—Preparation of methyl oleate by urea complexes.

Similar experiments have been carried out with methyl esters of corn oil, and in two preparations methyl linoleate has been isolated in 23% and 14% yields having iodine numbers of 168 and 173, respectively (theory 172.5). The use of urea complex formation for preparations of pure unsaturated fatty acids seems promising, and offers the advantage that no specialized equipment aside from a fractionating column is necessary, and the separations can be carried out without the aid of low temperatures. The scope of its usefulness is not as yet fully tested, and this will be the subject of further investigations.

Stabilization of Unsaturated Acids Against Oxidation.—It seemed probable that the solid complexes of unsaturated fatty acids should be different from the free acids with respect to autoxidation. This became apparent when the complexes of unsaturated acids did not develop the characteristic odor of rancidity upon standing in air. In experiments to test this, it was found that soybean fatty acids in complex form did not absorb oxygen, whereas the free acids oxidized rapidly.[12] The complex was formed from soybean fatty acids in a yield of 97%. After thorough washing and drying, some of the complex was decomposed to yield the free acids representative of the bound acids. Several 10-g. portions of the complex and 40 g. of the freed acids were exposed to air at room temperature and their peroxide values were determined periodically.[14] The results shown in Fig. 2 indicate that the fatty acids in the complex do not form peroxides.

The oxygen uptakes of pure linoleic and linolenic acids and their complexes were also compared. Samples of 87 mg. of these acids and 380 mg. samples of their complexes were exposed to oxygen at 37° with shaking in Warburg respirometer vessels. The results of these experiments shown in Fig. 3 indicate that the complexes do not absorb

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[12] H. Schlenk and R. T. Holman, *Science* **112**, 19 (1950).

[13] B. A. Brice and M. L. Swain, *J. Opt. Soc. Am.*, **35**, 532 (1945).

[14] D. H. Wheeler, *Oil and Soap*, **9**, 89 (1932).

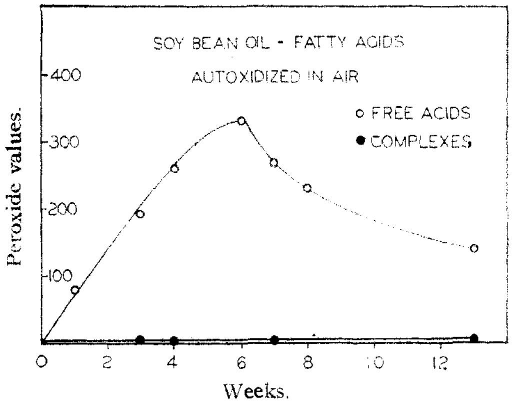

Fig. 2.—The development of peroxides in soybean fatty acids and in their complexes.

oxygen. Linoleic acid was recovered from its complex after standing one month in exposure to air, and the fatty acid was found to be unaltered. Its absorption spectrum showed no evidence of oxidation and it was found to be homogeneous in a single displacement chromatogram.[11] It is thus apparent from this evidence that easily oxidizable unsaturated compounds can be protected against autoxidation in the form of complex. The use of urea complexes might be of practical value in preserving such unstable unsaturated acids and esters in an easily handled form.

From the structure of urea complexes,[4] it is seen that the single fatty acid molecules occupy a restricted space within the crystal lattice of the urea. The crystal lattice probably offers a barrier against the free penetration of oxygen, and the restricted space within the lattice is too small to permit the formation of peroxide if oxygen were to penetrate. Furthermore, the autoxidation of unsaturated fatty acids is known to be a chain reaction, and it seems highly unlikely that such a mechanism could operate between the strictly separated fatty acid molecules in the crystal lattice. That is, contact of donor and acceptor molecules is prevented by the honeycomb structure of the urea complexes.

If urea complexes are to be used for protection against oxidation, it is desirable to convert the unsaturated acids to complex in good yield. The complex of linoleic acid has been prepared in 90% yield in the following manner: to 7.5 g. of linoleic acid in 30 ml. of methanol, 22.5 g. of powdered urea was added. The mixture was heated on a steam-bath with stirring. After three minutes of boiling, no more solid dissolved and the preparation was slowly cooled to room temperature, and placed in a refrigerator at −1° for several hours. The cold preparation was filtered and washed with 50 ml. of benzene on a Buchner funnel. The yield of complex was 26.7 g. having an acid value 50.6. Minor changes in procedure are necessary to form complexes of other acids or esters in good yield.

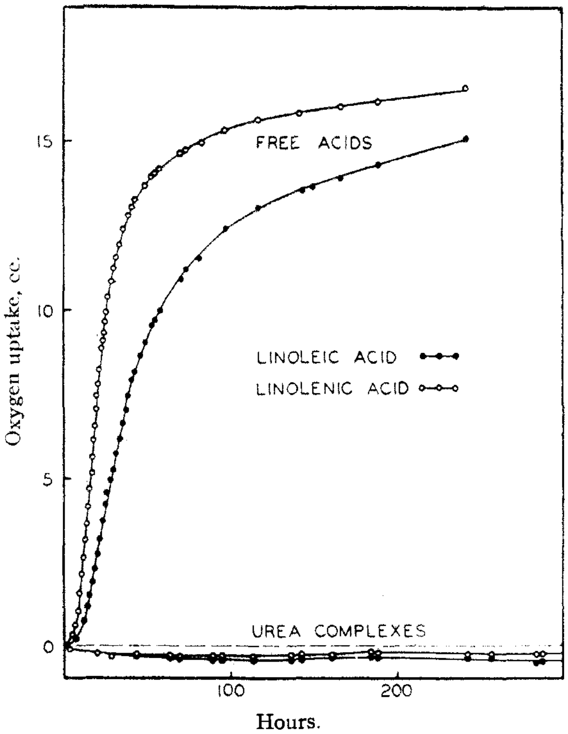

Fig. 3.—Oxygen absorption of linoleic and linolenic acids and their complexes at 37° under oxygen.

Summary

1. The urea addition complexes of a series of saturated and unsaturated acids have been prepared and analyzed.

2. Yields under standardized conditions can be used to predict separabilities of mixtures. The relationship between fatty acid structure and yield of complex is discussed.

3. Separations of typical model mixtures and natural mixtures are shown, and the preparation of methyl oleate by this method is outlined.

4. Urea complexes of unsaturated fatty acids are not subject to autoxidation.

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