Reconversion of 4-Hydroxy-axerophthene to Anhydrovitamin A_1.—Four drops of the HCl–chloroform reagent were added to a solution of 8 mg. of the hydroxy compound in 10 ml. of alcohol-free chloroform. Within 5 min. the liquid turned yellow. It was then transferred (with the aid of 20 ml. of hexane) into a separatory funnel. After the addition of water the epiphase was washed, dried and evaporated. The solution of the oily residue in a few ml. of hexane was developed on a 20 × 2 cm. magnesia–lime–Celite column (3:1:1). Below some minor pale zones the strongly orange fluorescent main zone (5 mm. thick) of the anhydrovitamin appeared; yield 1.25 mg. Spectral curve and adsorption behavior (magnesia–lime–Celite 3:1:1, hexane) were identical with a sample obtained by dehydrating crystalline vitamin A_1.

Acknowledgment.—The microanalyses were carried out by Dr. A. Elek in Los Angeles and Mr. G. Swinehart in Dr. Haagen-Smit's laboratory in Pasadena.

PASADENA, CALIFORNIA

[CONTRIBUTION FROM THE GENERAL RESEARCH ORGANIZATION, OLIN MATHIESON CHEMICAL CORP.]

The Position Isomerism of the Oleic Acid Formoxylation Reaction

BY JACK ROCKETT

RECEIVED NOVEMBER 2, 1955

The perchloric acid catalyzed addition of formic acid to oleic acid has been examined to determine the positions on the carbon chain to which the formoxy group becomes attached. *Via* a series of syntheses, a mixture of dibasic acids was obtained which, upon chromatographic separation, was shown to be a 50–50 molar mixture of azelaic and sebacic acids. The formic acid addition, therefore, takes place equally, and perhaps exclusively, at the 9- and 10-positions.

A recent paper[1] describes the perchloric acid catalyzed addition of formic acid to olefins. The addition to oleic acid resulted in a mixture of formoxystearic acids which, upon hydrolysis, gave a mixture of hydroxystearic acids of relatively high melting point. The ease with which 10-hydroxystearic acid could be obtained therefrom by repeated crystallizations led to the conjecture that the mixture must be essentially 9- and 10-hydroxystearic acids. The formoxylation of 1-hexene, however, gave, after hydrolysis, a mixture of 2- and 3-hexanol. No 1-hexanol could be found. The wandering of the point of addition in this reaction would lead one to suspect that the the formoxylation of oleic acid might have resulted in isomers other than 9- and 10-formoxystearic acids.

In order to determine the exact nature of the position isomers formed, the mixed hydroxystearic acids obtained as described by Knight, Koos and Swern,[1] was oxidized to a mixture of the corresponding keto-acids whose oximes were rearranged *via* the Beckmann rearrangement. The mixture of amides obtained thereby was hydrolyzed in an autoclave, and the hydrolysis products were separated by the method of Ross.[2] The mixture of dibasic acids was analyzed by elution chromatography through a silicic acid column.[3]

Three successive chromatograms were performed, giving an average value of 50.1 mole per cent. for sebacic acid and 49.9 mole per cent. for azelaic acid. A typical elution curve is shown in Fig. 1. Clearly two, and only two, dibasic acids were present in the mixture. The elution peaks were identified as sebacic and azelaic acids. The addition of formic acid to oleic acid takes place equally, therefore, at the 9- and 10-carbon positions. There appears to be no wandering from the site of the double bond.

In order to avoid loss of isomers, the entire

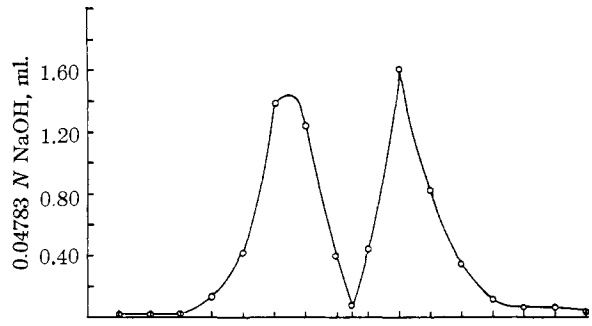


Fig. 1.—Titration of eluted samples from chromatographic column.

reaction product obtained in each step was used for the succeeding reaction. One recrystallization of ketostearic acid from acetone was found to be necessary in order to obtain a crystalline amide in the subsequent rearrangement. It is possible that isomers other than the 9- and 10-ketostearic acids were lost in this operation. The possibility of addition at positions other than C_9 and C_{10}, therefore, has not been completely eliminated. However, no trace of the existence of other isomers was found in the final mixture of dibasic acids.

It must be presumed that, although perchloric acid favors shifting of the carbonium ion from a primary to a secondary carbon atom (the 1-hexene addition), it does not cause any wandering of a secondary carbonium ion. This is in contrast to sulfuric acid which has been shown to do so.[4]

It is apparent, also, that there is neither an induced effect nor a field effect due to the carboxyl group at the end of the chain. Both 9- and 10-carbon atoms were perfectly equivalent in this reaction. This is in marked contrast to the hydrogenation of epoxystearic acid which is claimed to give only 10-hydroxystearic acid.[5]

(1) H. B. Knight R. E. Koos and D. Swern, THIS JOURNAL, **75**, 6212 (1953).

(2) J. Ross, A. I. Gebhart and J. F. Gerecht, *ibid.*, **71**, 285 (1949).

(3) T. Higuchi, N. C. Hill and G. B. Corcoran, *Anal. Chem.*, **24**, 491 (1952).

(4) B. B. Schaeffer, E. T. Roe, J. A. Dixon and W. C. Ault, THIS JOURNAL, **66**, 1924 (1944).

(5) C. H. Mack and W. G. Bickford, *J. Org. Chem.*, **18**, 686 (1953).

TABLE I

THE ETHYL ESTERS OF THE RESIDUAL ORGANIC ACIDS (10.0 G.)

Fraction	Head temp.	Press., mm.	Wt., g.	Sapn. no.	Possible monobasic acid ethyl esters	Sapn. no.	Possible dibasic acid diethyl esters	Sapn. no.
1	51–62°	0.1	0.6	293	Nonanoate	301	Suberate	487
2	62–105	.1	0.5	289			Azelate	458
3	105–122	.1	1.6	277	Decanoate	280	Sebacate	433
4	122–142	.1	2.0	261	Palmitate	197	Undecanedioate	412
5	167–174	.7	2.3	182			Dodecanedioate	393
6	174	.7	1.2	181	Stearate	181	Tridecanedioate	374
		Residue	1.4					

The isolation of the dibasic acids was performed *via* the extraction of the organic acids with successive portions of boiling water. Since this method might conceivably have failed to extract the higher molecular weight dibasic acids, a portion of the residual material was esterified with ethanol and distilled through a 9-inch Vigreux head. The individual fractions were then examined for their saponification numbers. As shown in Table I, the values range, in regular fashion, from 293 to 181. Also shown are the saponification numbers of possible dibasic acid esters and those for the expected monobasic acid esters. The good agreement with the values for the monobasic series indicates that the acids present in the residue are, indeed, only monobasic ones.

Experimental

9- and 10-Formoxystearic Acids.—In a flask equipped with a nitrogen inlet was placed 588 g. (1.87 moles) of commercial oleic acid,[6] 1000 ml. of 98–100% formic acid and 6 ml. of 70% perchloric acid. The mixture was heated and stirred while nitrogen was bubbled in. When the reflux temperature was reached (105°), it was maintained for 15 minutes. The formic acid was distilled at reduced pressure and the oil residue was washed with hot water to *p*H 4.0. The oil was dried over anhydrous sodium sulfate and filtered. There was obtained 660 g. of a clear red oil. The crude product was used without purification.

Anal. Calcd. for $C_{17}H_{34}(OOCH)COOH$: I.V., 0. Found: I.V., 16.

9- and 10-Hydroxystearic Acids.—In a flask, 300 g. of the crude mixture of formoxystearic acids was hydrolyzed with 350 cc. of 6 *N* potassium hydroxide. The hydrolyzate was poured into an excess of 1:1 hydrochloric acid and the separated oil, after cooling to a solid cake, was washed several times by boiling with large amounts of water. The crude hydroxystearic acid weighed 277.3 g. A small amount was recrystallized once from ligroin, m.p. 66–70°.

Anal. (Crude product) Calcd. for $C_{17}H_{34}(OH)COOH$: I.V., 0; hydroxyl O, 5.32. Found: I.V., 23; hydroxyl O, 3.86.

9- and 10-Ketostearic Acids.—A mixture of 249.2 g. of the crude hydroxystearic acid mixture, 0.63 mole by analysis, and 415 g. of glacial acetic acid was kept at 32° as a solution of 58.2 g., 0.582 mole, of chromic acid dissolved in a solution of 830 g. of acetic acid plus 40 cc. of water, was added dropwise. The addition took two hours. Thereafter the solution was kept at 35–40° for another 1.5 hours. The flask contents were poured into 3 liters of water, the solid product was collected, heated to boiling with 2 liters of 1:1 hydrochloric acid and, after decanting the green aqueous solution, boiled with distilled water. The crude product separated upon cooling, wt. 231.0 g. A 220.8-g. sample was recrystallized from 500 cc. of acetone, giving 150.2 g. of crystallized product.

Anal. Calcd. for $C_{17}H_{33}(O)COOH$: carbonyl O, 5.35. Found: carbonyl O, 4.7.

Since the carbonyl analysis was 3.9% for the crude material, the actual loss of carbonyl compound during the recrystallization was 18.0% of the original content.

(6) This grade is claimed to be 87% oleic acid, 5% linoleic acid and 8% saturated fatty acids.

The Oximes of Ketostearic Acids.—To 100.0 g., 0.294 mole, of the mixture of ketostearic acids, 25.6 g., 0.369 mole, of hydroxylamine hydrochloride, and 1200 cc. of ethanol, was added a solution of 64.8 g., 1.005 moles, of potassium hydroxide dissolved in 240 cc. of water. The mixture was stirred at reflux temperature for six hours. The ethanol and water were distilled, at reduced pressure, from a steam-bath. When it had nearly all been distilled about 500 cc. of water plus 35 cc. of hydrochloric acid was added. The distillation of alcohol was continued, and, when it was completed, 25.0 cc. more of hydrochloric acid was added. The organic material was ether extracted, washed with water, and the ether solution was dried over anhydrous sodium sulfate. The ether was filtered and distilled. There remained 105.4 g. of a clear orange oil.

Anal. Calcd. for $C_{17}H_{33}(NOH)COOH$: N, 4.5. Found: N, 3.13.

The Beckmann Rearrangement.—The crude oxime mixture was heated by steam-bath to 85° and 205 cc. of 93% sulfuric acid was added dropwise. The temperature was regulated at 85–90°. When the addition was complete, it was heated at 95° for another hour. The dark brown oil was poured on ice and, upon cooling, the water was decanted and the oil was re-boiled with fresh water. This was repeated five times until the aqueous residue reached a *p*H of 4.5. The crude brown wax weighed 100.3 g., a 97.8% crude yield.

Anal. Calcd. for $C_{16}H_{33}(NHCO)COOH$: N, 4.5. Found: N, 3.15.

Hydrolysis of the Amides.—Into an autoclave was placed 97.5 g. of the crude amide mixture plus 400 cc. of 20% potassium hydroxide. The contents were heated, with stirring, to 180–190° for four hours.

Monobasic Acids.—The bomb contents were transferred, 138 cc. of concd. hydrochloric acid was added, and the solution was steam distilled until no more oily droplets distilled. The distillates were ether extracted, dried and distilled. There was obtained 18.4 g. of a clear yellow oil, a 35.9% yield.

Anal. Calcd. for nonanoic acid: neut. equiv., 158. Calcd. for decanoic acid: neut. equiv., 172. Found: neut. equiv., 161.

Dibasic Acids.—The residue left from the steam distillation was extracted with ether. Distillation of the ether left a brown wax weighing 44.0 g. It was extracted with three successive portions of boiling water, a total of 350 cc., and filtered hot. Upon cooling, the white crystalline deposits were filtered and dried to constant weight in a vacuum desiccator; wt. 20.8 g., 0.107 mole, a 34.3% yield.

Anal. Calcd. for azelaic acid: neut. equiv., 94. Calcd. for sebacic acid: neut. equiv., 101. Found: neut. equiv., 98.

The Chromatographic Separation.—A 0.1601-g. sample of the dibasic acids was dissolved in 1.25 ml. of *t*-amyl alcohol and diluted to 25.0 ml. with chloroform. A 5.0-ml. sample was pipetted into a column, prepared according to the method of Higuchi, and eluted with successive 10-cc. portions of solvent.[3] The eluted 10.0-cc. portions were titrated with 0.04783 *N* alcoholic sodium hydroxide. The chromatogram is shown in Fig. 1.

To positively identify the acids represented by each "peak," fractions 4 through 8 were combined after titration. They were evaporated to dryness by a stream of air. The solid residue, dissolved in 1 cc. of water, was placed in a tube with a solution of 0.023 g. of *p*-bromophenacyl bromide in 1 cc. of alcohol and the tube was sealed and heated in a 90–95° bath for an hour. It was cooled, opened, and filtered;

m.p. 139–143°. It was recrystallized once from 0.5 cc. of ethyl alcohol and the crystals dried on a porous plate; m.p. 143–147°. The literature value for the di-*p*-bromophenacyl ester of sebacic acid is 147°.

The titrated fractions 10 through 16 were combined and evaporated to dryness. The solid residue was dissolved in 1 cc. of water to which was added 0.06 g. of *p*-bromophenacyl bromide dissolved in 2 cc. of ethanol. It was heated under reflux for two hours. A fine crystalline material was filtered and dried; m.p. 131°. An authentic sample of the di-*p*-bromophenacyl ester of azelaic acid was prepared; m.p. and mixed m.p. 131°.

Acknowledgment.—The author is indebted to Dr. Paul Sternglanz and Miss Vera Jane Wilson for the analyses reported in this work.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

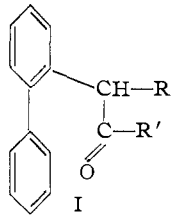
Aromatic Cyclodehydration. XXXII.[1] Loss of the Isopropyl Group on Cyclodehydration[2]

BY CHARLES K. BRADSHER AND DOROTHY J. BEAVERS[3]

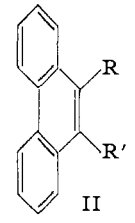
RECEIVED NOVEMBER 19, 1955

A direct and unambiguous synthesis of 9-isopropyl-10-methylphenanthrene (XI) has been accomplished. The instability of this hydrocarbon in the presence of boiling hydrobromic and acetic acids offers adequate explanation for the loss of isopropyl groups observed during the aromatic cyclodehydration of certain ketones and olefin oxides.

In an earlier communication[4] it was demonstrated that cyclodehydration of ketones of type I where R or R′ was the isopropyl group resulted in the elimination of the isopropyl group at some



I



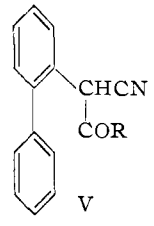
II

stage in the reaction yielding a 9-alkylphenanthrene II (R or R′ = H). It was also shown that an olefin oxide which might be expected to yield 9-isopropyl-10-isobutylphenanthrene afforded instead 9-isobutylphenanthrene.

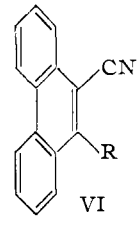
As was suggested earlier,[4] it seemed important to determine first whether 9-isopropyl-10-alkylphenanthrene (II, R = $CH(CH_3)_2$) would be stable in the boiling hydrobromic–acetic acid mixture used in the cyclization procedure. Since 9-methylphenanthrene crystallizes well and could be easily isolated from the "deisopropylation" experiment, the synthesis of 9-methyl-10-isopropylphenanthrene (II, R = CH_3, R′ = $CH(CH_3)_2$) was undertaken. Several unsuccessful attempts were made, but only two appear worthy of mention.

Syntheses starting from 10-bromo-9-methylphenanthrene (III)[5,6] appeared promising, but the hydrocarbon obtained in 23% yield by addition of isopropyl iodide to the lithium reagent formed from III by exchange with butyllithium proved to be 9-methyl-10-butylphenanthrene (IV).[4] Reaction of the same lithium reagent with acetone gave no identifiable addition product.

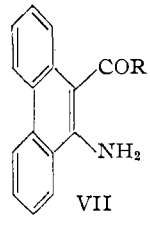
Previously[7] it has been found that α-acetyl- and α-propionyl-(2-biphenylyl)-acetonitriles (V, R = CH_3, C_2H_5) undergo cyclodehydration in the presence of boiling hydrobromic and acetic acids to yield 9-alkyl-10-phenanthronitrile (or the corresponding amide). Acylation of biphenylylacetonitrile with ethyl isobutyrate afforded the α-isobutyro-(2-biphenylyl)-acetonitrile (V, R = $(CH_3)_2CH$) in 63% yield. Unlike the lower homologs, V (R = CH_3, C_2H_5), the isobutyronitrile, when refluxed with hydrobromic and acetic acids, afforded only the corresponding hydrocarbon, 9-isopropylphenanthrene. Cyclization is slower with the larger, branched alkyl group so that hydrolysis of the nitrile group and decarboxylation of the resulting acid can occur prior to cyclization. A parallel observation has been made with α-benzoyl-(2-biphenylyl)-acetonitrile.[8]



V



VI



VII

With concentrated sulfuric acid the isobutyronitrile V (R = $(CH_3)_2CH$) cyclized to yield the desired 9-isopropyl-10-phenanthronitrile (54.5% yield) rather than 10-isobutyro-9-phenanthrylamine (VII, R = $(CH_3)_2CH$). The amine would have been expected if the nitrile group had excelled the carbonyl group in rate of attack on the adjacent phenyl group.[9] Under the same conditions the corresponding propionylacetonitrile V (R = C_2H_5) was found to cyclize to 9-ethyl-10-phenanthronitrile (VI, R = C_2H_5), in about the same yield. It was found that polyphosphoric acid was effective

(1) For the preceding communication of this series, see C. K. Bradsher and L. E. Beavers, THIS JOURNAL, **78**, 2459 (1956).

(2) This investigation was supported in part by a research grant (C-1743) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

(3) Abstracted from a dissertation submitted in partial fulfillment of the degree of Doctor of Philosophy, 1955.

(4) C. K. Bradsher and W. J. Jackson, Jr., THIS JOURNAL, **76**, 4140 (1954).

(5) B. M. Mikhailov and N. G. Chernova, *J. Gen. Chem. of U.S.S.R.*, **21**, 1659 (1951).

(6) P. Lambert and R. H. Martin, *Bull. soc. chim. Belges*, **61**, 31 (1952).

(7) C. K. Bradsher and W. J. Jackson, Jr., THIS JOURNAL, **76**, 734 (1954).

(8) C. K. Bradsher and R. S. Kittila, *ibid.*, **72**, 277 (1950).

(9) C. K. Bradsher and D. J. Beavers, *ibid.*, **78**, 2153 (1956).