aqueous methanol gave 0.030 g. (30%) of 3α,12α-dihydroxy-5β-etianic acid, and 0.035 g. (35%) of the 12β-isomer. There was also obtained 0.005 g. of a mixture of the two compounds.

When the reduction was repeated using 0.1 g. of keto acid, the crude product was methylated to give 0.0543 g. of ester, $[\alpha]^{25}\mathrm{D}$ +37° (c 0.543, chloroform). This corresponds to 32 and 68% of the 12α- and 12β-hydroxy compounds, respectively.

Rockogenin-3-tetrahydropyranyl Ether. A.—To a solution of 3 g. of sodium borohydride in 30 ml. of methanol was added 1.0 g. of hecogenin-3-tetrahydropyranyl ether and the resulting mixture was heated at reflux for 1 hr. The reaction mixture was cooled, diluted with water, acidified with 5% hydrochloric acid, and extracted with methylene chloride. The organic extract was washed with water and dried; the solvent was removed *in vacuo*, leaving a crystalline residue. Recrystallization from acetone gave 0.71 g. (71%) of white crystals, m.p. 235–236°, $[\alpha]^{25}\mathrm{D}$ −39.6° (chloroform).

Anal. Calcd. for $C_{32}H_{52}O_5$: C, 74.37; H, 10.24. Found: C, 74.18; H, 10.32.

B.—A solution of 6.0 g. of the hecogenin derivative in 70 ml. of a 1:1 methanol–ether mixture was added with stirring to 200 ml. of liquid ammonia. Over a period of 1 hr., 6.0 g. of lithium in small pieces was added, and finally 96 g. of ammonium chloride was added slowly. The reaction mixture was allowed to come to room temperature, and then warmed gently until the ammonia had evaporated. The solid residue was taken up in water and chloroform; the organic layer was drawn off, washed with dilute hydrochloric acid and 5% aqueous sodium bicarbonate, and dried; and the solvent was removed at reduced pressure. The solid residue was recrystallized from acetone to give 4.50 g. (75%) of white crystals, m.p. 235–236°, undepressed on mixing with material prepared by method A.

C.—To a solution of 2.1 g. of hecogenin-3-tetrahydropyranyl ether in 200 ml. of *n*-propyl alcohol was added, over a period of 1 hr., 20 g. of sodium, and the solution was heated at reflux for 1 hr. After cooling, the reaction mixture was poured into water and extracted twice with chloroform. The chloroform extracts were washed with water and dried; the solvent was removed *in vacuo* leaving a tan solid. Recrystallization from acetone gave 1.19 g. (57%) of rockogenin-3-tetrahydropyranyl ether, m.p. 235–236°.

Chromic Acid Oxidations.—To 5.00-ml. portions of 1.89×10^{-3} *M* chromic acid in 90.0% acetic acid in a spectrophotometer cell at 25 ± 1° were added 3.00 ml. of $1.5\text{–}2.0 \times 10^{-3}$ *M* solutions of the alcohol, and the decrease in intensity of the chromate absorption with respect to time was determined, employing a Beckman Model B spectrophotometer. In each run at least five points were taken, at approximately 2-min. intervals. The rate constants were calculated using the following equation.

$$\frac{-d[\mathrm{Cr(VI)}]}{dt} = k[\mathrm{Cr(VI)}][\mathrm{ROH}]$$

This simplifies to the standard second-order rate expression.

$$k = \frac{2.3}{([\mathrm{Cr}]_0 - [\mathrm{ROH}]_0)t} \log \frac{[\mathrm{ROH}]_0[\mathrm{Cr}]_t}{[\mathrm{Cr}]_0\,[\mathrm{ROH}]_t}$$

The results are summarized in Table II.

TABLE II

Compd.	Concn., $M \times 10^3$	k (moles/l./min. $\times 10^{-6}$)
Cyclohexanol	0.825	0.312 ± 0.045
12β-Cholanol (run 1)	0.609	1.42 ± 0.24
(run 2)	0.609	1.50 ± 0.17
12α-Cholanol (run 1)	0.659	3.06 ± 0.16
(run 2)	0.659	3.39 ± 0.03
Rockogenin-3β-methyl succinate		
(run 1)	0.680	1.31 ± 0.14
(run 2)	0.680	1.42 ± 0.13

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Huang-Minlon Reduction of Acetylenic Keto Acids

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Huang-Minlon reduction of 7-keto-16-heptadecynoic acid as well as 7-keto-15-heptadecynoic acid gave 16-ketoheptadecanoic acid along with heptadecanoic acid. Treatment of 10-undecynoic acid with strong alkali both in the presence and absence of hydrazine hydrate afforded 10-ketoundecanoic acid. These observations would possibly be explained by assuming alkaline hydration of the acetylenic triple bond. A preparation of *cis*-15-heptadecenoic acid was described.

In a previous Note[1] the migration of terminal double bond under the strongly alkaline condition was described. When 7-keto-16-heptadecenoic acid was subjected to the Huang-Minlon reduction, an isomeric mixture of 15-heptadecenoic acids was obtained. Similar result was also reported by Hünig and Eckart,[2] and according to them 16-heptadecenoic acid could be obtained by substituting triethanolamine[3] for diethylene glycol as the solvent.

The present investigation was aimed at elucidating the behavior of ω-acetylenic keto acid in the Huang-Minlon reduction and preparing *cis*-15-heptadecenoic acid.

The reaction of 10-undecynoyl chloride (I) with N-(1-cyclohexenyl)morpholine (II) was effected similarly as described before[1] and 7-keto-16-heptadecynoic acid (III) was obtained in 81% yield. On the analogy of the olefinic compound, the Huang-Minlon reduction of III would result in the formation of 15-heptadecynoic acid (IV), since the migration of the terminal acetylenic triple bond along the carbon chain caused by strong alkali has been recognized by several workers.[4] When III was treated with alkali and hydrazine hydrate in diethylene glycol, two kinds of reaction products (V and VI) were isolated in a ratio of about 1:10. Both were proved to be carboxylic acids, but they had no absorption maxima responsible for the presence of an acetylenic triple bond.

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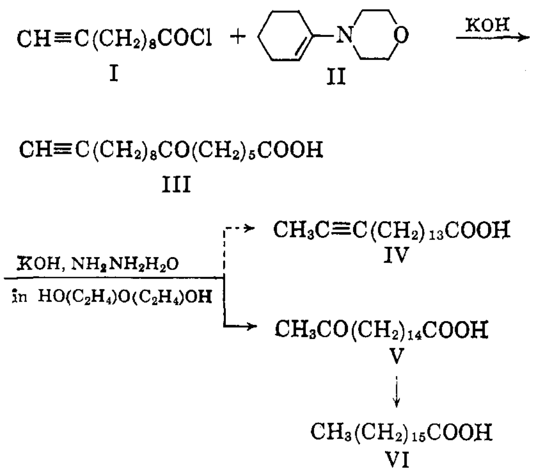
(1) K. Sisido and M. Kawanisi, *J. Org. Chem.*, **27**, 3722 (1962).

(2) S. Hünig and W. Eckart, *Chem. Ber.*, **95**, 2493 (1962).

(3) *Cf.* P. D. Gardner, L. Rand, and G. R. Hyanes, *J. Am. Chem. Soc.*, **78**, 3425 (1956).

(4) (a) R. G. Ackman, R. A. Dytham, B. J. Wakefield, and B. C. L. Weedon, *Tetrahedron*, **8**, 239 (1960); (b) E. S. Stenhagen, *Arkiv Kemi*, **1**, 99 (1949); (c) G. Eglington, E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 3197 (1954); (d) E. R. H. Jones, G. H. Whitham, and M. C. Whiting, *ibid.*, 3201 (1954); (e) F. Krafft, *Ber.*, **29**, 2232 (1896); (f) T. L. Jacobs, R. Akawie, and R. G. Cooper, *J. Am. Chem. Soc.*, **73**, 1273 (1951); (g) T. L. Jacobs, *Org. Reactions*, **5**, 13 (1949).



VI was determined as heptadecanoic acid by analysis as well as mixture melting point with an authentic sample prepared from undecanoyl chloride and II *via* the saturated keto acid.

The acid V had a molecular formula, $C_{17}H_{32}O_3$, and gave semicarbazone. This compound was established as 16-ketoheptadecanoic acid by mixture melting point with an authentic sample and the comparison of the spectral data.

The synthesis of V was carried out starting from 16-heptadecenoic acid[2] (VII), the double bond of which was verified by comparing with an unsaturated acid derived from 14-pentadecenoic acid[5] by the malonic ester homologation. Bromination of VII followed by dehydrobromination afforded 16-heptadecynoic acid (VIII). This was hydrated with formic acid in the presence of mercuric sulfate[6] to give V.

A similar reaction of 9-undecynoyl chloride (IX) with II gave 7-keto-15-heptadecynoic acid (X). Reduction of X in a similar fashion afforded also V and VI. Likewise the formation of IV was not observed.

When semicarbazone of III was treated with alkali[7] in diethylene glycol, V was obtained as a sole identified product.

$$\underset{\text{VII}}{CH_2{=}CH(CH_2)_{14}COOH} \longrightarrow \underset{\text{VIII}}{CH{\equiv}C(CH_2)_{14}COOH} \xrightarrow[\text{HgSO}]{\text{HCOOH}} \text{V}$$

$$\underset{\text{IX}}{CH_3C{\equiv}C(CH_2)_7COCl} + \text{II} \longrightarrow$$

$$\underset{\text{X}}{CH_3C{\equiv}C(CH_2)_7CO(CH_2)_5COOH} \longrightarrow \text{V} \longrightarrow \text{VI}$$

The fact that III gave keto acid V and saturated acid VI would claim the hydration of the triple bond under the strongly alkaline condition to give a ketonic group which would further be reduced with excess hydrazine. Although the reduction of triple bond with hydrazine has been recognized in the presence of an oxidizing catalyst such as atmospheric oxygen,[8] this probability might be excluded in the present investigation, as the reaction was conducted under nitrogen atmosphere at relatively high temperature; therefore solubility of atmospheric oxygen in the reaction medium might be considered to be infinitesimal.[8] The hydration of acetylenic triple bond under acidic condition, especially in the presence of heavy metal catalyst, is a familiar method of synthesizing the corresponding carbonyl compound.[9] However, few have been reported about the basic hydration of the triple bond. The assumed hydration of 3-butynoic and 3-pentynoic acids may be cited for example.[4d] Ackman and co-workers[4a] reported that 10-undecynoic acid gave lower homologous saturated acid with loss of four carbon atoms when treated under the so-called Varrentrapp reaction, but they did not refer to the formation of keto acid.

In order to obtain further information about the action of alkali over acetylenic bond, the reaction of 10-undecynoic acid with potassium hydroxide in diethylene glycol at 200° was investigated in the presence and absence of hydrazine hydrate. In both cases 10-ketoundecanoic acid was isolated and identified. In the absence of hydrazine, a relatively large amount of the keto acid was obtained, while in the presence of hydrazine a large amount of undecanoic acid was presented in the reaction products. These observations might support the mechanism for the reaction of III.

cis-15-Heptadecenoic acid was prepared from 15-heptadecenoic acid, prepared previously,[1] by bromination and dehydrobromination followed by hydrogenation over Lindlar catalyst.[10] The yield was almost quantitative.

Experimental[11]

7-Keto-16-heptadecynoic Acid (III).—To a mixture of 28.0 g. of N-(1-cyclohexenyl)morpholine (II)[12] and 18.7 g. of triethylamine in 200 ml. of chloroform was added gradually a solution of 31.0 g. of 10-undecynoyl chloride, b.p. 151–153° at 28 mm. (lit.[13] b.p. 135° at 15 mm.) in 80 ml. of chloroform in the course of 1 hr. at 35°. Usual work-up[1] gave 25.0 g. (81%) of III, m.p. 71.0–71.5° (from *n*-hexane), ν_{max} (Nujol) 3320 and 2120 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C 72.93; H, 10.23.

Semicarbazone prepared by the conventional method[14] melted at 104.8–105.3° after a recrystallization from ethanol.

Anal. Calcd. for $C_{18}H_{31}N_3O_3$: C, 64.06; H, 9.26. Found: C, 64.41; H, 9.41.

Reaction of III under Huang-Minlon Condition.—A mixture of 18.0 g. of III, 3.6 g. of potassium hydroxide, 28 ml. of 80% hydrazine hydrate, and 65 ml. of diethylene glycol was heated under reflux for 8 hr. To the hot solution was added 18.0 g. of potassium hydroxide and 65 ml. of diethylene glycol, and water as well as excess hydrazine hydrate were removed by distillation. The temperature of the contents was allowed to rise gradually to 185°, when the mixture was heated under reflux for an additional 15 hr. The reaction mass was poured into 1 l. of water, acidified with concentrated hydrochloric acid, and extracted with ether. The ethereal solution was washed with water and dried ($MgSO_4$). Evaporation of ether followed by distillation *in vacuo* gave a distillate (15.0 g.) which solidified immediately. This was fractionally recrystallized from *n*-pentane into 12.0 g. of soluble portion (VI), m.p. 45–67°, and 0.8 g. of a sparingly soluble portion (V), m.p. 82–83°. Two recrystallizations of VI from ethanol gave colorless leaflets, m.p. 61.5–62.5°. Analyses gave values of $C_{17}H_{34}O_2$. No absorption was observed in 3300-cm. $^{-1}$ region. Mixture melting point with heptadecanoic acid, m.p. 61.5–62.5°, described in the following section, was 61.5–62.5°. Two recrystallizations of V from acetone furnished colorless scales, m.p. 85.0–85.4°.

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(5) P. Chuit, F. Boelsing, J. Hausser, and G. Malet, *Helv. Chim. Acta*, **10**, 127 (1927).

(6) A. Mondon, *Ann.*, **590**, 43 (1954).

(7) *Cf.* D. Todd, *Org. Reactions*, **4**, 390 (1948).

(8) F. Aylward and M. Sawestoska, *Chem. Ind.* (London), 484 (1962) S. Hünig, H. R. Müller, and W. Their, *Tetrahedron Letters*, 353 (1960).

(9) R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Buttherworth and Co. (Publishers) Ltd., London, England, 1955, p. 40.

(10) H. Lindlar, *Helv. Chim. Acta*, **35**, 446 (1952).

(11) Microanalyses were performed by Miss Kenko Ogawa of this laboratory.

(12) S. Hünig, E. Lücke, and W. Brenninger, *Org. Syn.*, **41**, 65 (1961).

(13) E. G. Popova and M. Ya. Kraft, *Chem. Abstr.*, **55**, 7395 (1961).

(14) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 218.

Anal. Calcd. for $C_{17}H_{32}O_3$: C, 71.87; H, 11.49. Found: C, 71.78; H, 11.34.

No absorption was observed in the 3300-cm.$^{-1}$ region. Mixture melting point with an authentic specimen of 16-ketoheptadecanoic acid, m.p. 85.0– 85.5°, described in the susequent section was 85.0–85.5°. Semicarbazone[14] melted at 138.7–139.2° after recrystallizations from ethanol.

Anal. Calcd. for $C_{18}H_{35}N_3O_3$: C, 63.31; H, 10.33. Found: C, 63.49; H, 10.55.

Heptadecanoic Acid.—The reaction of 48.5 g. of undecanoyl chloride, b.p. 153–155° at 48 mm. (lit.[15] b.p. 119–120° at 10 mm.), with 43.3 g. of II was effected analogously and 35.8 g. (86%) of 7-ketoheptadecanoic acid, m.p. 78.0–79.0°, was obtained after two recrystallizations from *n*-hexane.

Anal. Calcd. for $C_{17}H_{32}O_2$: C, 71.78; H, 11.34. Found: C, 72.04; H, 11.38.

Semicarbazone,[14] m.p. 123.0–124.0°, was obtained from ethanol.

Anal. Calcd. for $C_{18}H_{35}N_3O_3$: C, 63.31; H, 10.33. Found: C, 63.44; H, 10.49.

The reduction of 21.6 g. of aforementioned keto acid was conducted analogously as described above and 19.5 g. of *n*-heptadecanoic acid was obtained: m.p. 61.5–62.0° (lit.[16] m.p. 61.3°) after recrystallizations from methanol.

16-Heptadecenoic Acid from 14-Pentadecenoic Acid.—This preparation followed essentially the published one described for 12-tridecenoic acid from 10-undecenoic acid.[17] A reaction of 11.2 g. of 14-pentadecenoic acid[5] with 8.4 g. of thionyl chloride gave 8.5 g. of 14-pentadecenoyl chloride, b.p. 143–144° (3 mm.), which was gradually introduced into 30 ml. of methanol with vigorous agitation. Extraction with ether followed by evaporation of ether afforded 7.5 g. of methyl 14-pentadecenoate: b.p. 129–130° at 2.5 mm. (lit.[5] b.p. 167–168° at 8 mm.); $n^{18}\mathrm{D}$ 1.4476; ν_{max} (liquid film) 3070, 1640, 990, and 910 cm.$^{-1}$. Lithium aluminum hydride reduction[18] of 7.5 g. of the methyl ester gave 6.0 g. of 14-pentadecenol: m.p. 32–34° (lit.[5] m.p. 32–33°); ν_{max} (liquid film) 3290, 3070, 1640, 990, and 910 cm.$^{-1}$. This unsaturated alcohol was converted into 14-pentadecenyl chloride by means of thionyl chloride and pyridine in benzene and unsaturated chloride [b.p. 135–137° at 2.5 mm.; $n^{16}\mathrm{D}$ 1.4574; ν_{max} (liquid film) 3070, 1640, 990, and 910 cm.$^{-1}$] was obtained in 74% yield. A reaction of 4.8 g. of the unsaturated chloride with diethyl sodiomalonate (from 3.5 g. of diethyl malonate and 0.6 g. of sodium) in the presence of 0.8 g. of sodium iodide was conducted according to the published procedure.[17] The resulted alkenylmalonic ester was hydrolyzed and decarboxylate to give 1.0 g. of 16-heptadecenoic acid, m.p. 57–58°, after two recrystallizations from *n*-hexane. This gave correct analyses for carbon and hydrogen; ν_{max} (Nujol) 1640, 990, and 910 cm.$^{-1}$. Alternatively, 15.5 g. of 7-keto-16-heptadecenoic acid[1] was treated exactly in the same manner as described by Hunig[2] and 13.8 g. of crude 16-heptadecenoic acid, m.p. 54–56°, was obtained. This gave colorless leaflets melting at 56.7–57.5° after recrystallizations from *n*-hexane: ν_{max} (Nujol) 1640, 990, and 910 cm.$^{-1}$. Mixture melting point with the specimen described in the previous section was 57.0–58.0°.

16-Heptadecynoic Acid (VIII).—To a cooled solution of 11.0 g. of 16-heptadecenoic acid in 200 ml. of hexane and 100 ml. of chloroform was added 8.0 g. of bromine, maintaining the temperature below −8°, and excess bromine was removed by suction. Evaporation of the solvent under diminished pressure below 40° gave 17.5 g. of crude bromide, m.p. 48–51°, which was purified recrystallization from *n*-hexane to furnish colorless leaflets, m.p. 61.0–62.0°. This bromide was immediately submitted to dehydrobromination. A mixture of 17.5 g. of dibromide, 10.0 g. of potassium hydroxide, and 70 ml. of ethanol was refluxed with vigorous stirring for 24 hr. After evaporation of ethanol, the residue was dissolved into 100 ml. of water and acidified with hydrochloric acid. Usual work-up gave 10.0 g. of crude acid, m.p. 53–56°, which melted at 74–75° after two recrystallizations from *n*-hexane: ν_{max} (Nujol) 3300 and 2120 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.55; H, 11.35.

16-Ketoheptadecanoic Acid (V).—A mixture of 2.0 g. of VIII, 0.1 g. of mercuric sulfate, and 15 ml. of 80% formic acid was heated at 100° for 2 hr. Evaporation of formic acid under reduced pressure gave a solid residue which was taken up in ether. Ethereal solution was washed with saturated aqueous sodium chloride solution and dried ($MgSO_4$). Evaporation of ether gave 1.0 g. (47%) of crude product, m.p. 82–83°, which melted at 85.0–85.5° after two recrystallizations from acetone and did not depress the melting point when admixed with the specimen obtained from III.

Anal. Calcd. for $C_{17}H_{32}O_3$: C, 71.78; 11.34. Found: C, 71.96; H, 11.30.

7-Keto-16-heptadecyanoic Acid (X).—9-Undecynoic acid, m.p. 56–59° (lit.[19] m.p. 60.5–61°), was converted by means of thionyl chloride into 9-undecynoyl chloride, b.p. 138–140° (14 mm.), in 86% yield: ν_{max} (liquid film) 1790 cm.$^{-1}$. A reaction of 37.5 g. of 9-undecynoyl chloride with II was conducted in a similar manner as described for the 10-isomer, and 38.0 g. (89%) of crude keto acid which melted at 72.5–73.5° after three recrystallizations from petroleum ether (b.p. 60–80°) was obtained.

Anal. Calcd. for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.89; H, 10.15.

Semicarbazone[14] melted at 101.4–102.3° after a single recrystallization from ethanol.

Anal. Calcd. for $C_{18}H_{31}N_3O_3$: C, 64.06; H, 9.26. Found: C, 64.21; H, 9.42.

Reaction of 7-Keto-16-heptadecynoic Acid (X) under Huang-Minlon Condition.—Reduction of 15.0 g. of X under the Huang-Minlon reaction condition was effected similarly as described for III, and 11.5 g. of semisolid reaction product resulted. This was separated by fractional recrystallization from *n*-pentane into 8 g. of soluble portion, m.p. 45–65°, and 0.8 g. of sparingly soluble portion, m.p. 83–85°. The former was purified by recrystallization from methanol and there were obtained colorless scales, m.p. 61.0–62.0°, which showed no melting point depression when admixed with VI. The latter melted at 84.5–85.5° after recrystallization from acetone and also did not depress the melting point when admixed with V.

Alkaline Treatment of the Semicarbazone of III.—A mixture of 5 g. of the semicarbazone of III and potassium hydroxide in 35 ml. of diethylene glycol was heated under nitrogen atmosphere at 200° for 20 hr. The extensive darkening of the reaction mixture was observed in this case. The reaction mixture was poured into 300 ml. of water and acidified with concentrated hydrochloric acid and extracted with ether. Evaporation of ether gave dark-colored, solid residue which was distilled *in vacuo*. The fraction boiling at 150–200° (2 mm.) and weighing 2 g. gradually deposited 0.5 g. of solid material. This was separated by filtration and recrystallized from acetone to give colorless leaflets, m.p. 84.5–85.5°, *identical* with V.

Alkaline Treatment of 10-Undecynoic Acid in Diethylene Glycol. A. In the Absence of Hydrazine Hydrate.—A mixture of 10.0 g. of 10-undecynoic acid[20] and 3 g. of potassium hydroxide in 54 ml. of diethylene glycol was heated at 129–130° under reflux for 8 hr. Successively 15 g. of potassium hydroxide and 74 ml. of diethylene glycol were added and water was removed by distillation rapidly until inner temperature became 200°, when the mixture was heated under reflux for an additional 15 hr. The hot reaction mass was poured into 1 l. of water and acidified with hydrochloric acid and extracted with ether. Evaporation of ether followed by distillation *in vacuo* afforded 7.1 g. of colorless oil, boiling at 130–172° (3 mm.), from which 2.7 g. of solid substance separated. The solid melted at 58.0–59.0° after recrystallizations from *n*-pentane, and did not depress the melting point when admixed with an authentic specimen of 10-ketoundecanoic acid, m.p. 59.2–60.0° (lit.[21] m.p. 59.5°). The mother liquor, freed from the solid material, was added with an excess solution of 2,4-dinitrophenylhydrazine[22] and a reddish orange crystalline product, m.p. 69.0–70.0°, was obtained. This did not depress the melting point when admixed with a specimen of 2,4-dinitrophenylhydrazone of 10-ketoundecanoic acid. Alternatively the above liquid was converted into methyl ester by means of diazomethane and analyzed by gas chromatography, when the presence of methyl 10-ketoundecanoate was re-established.

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(15) H. F. Fierz-David and W. Kuster, *Helv. Chim. Acta*, **22**, 89 (1939).

(16) A. W. Ralston, "Fatty Acids and Their Derivatives," John Wiley and Sons Inc., New York, N. Y., 1956, p. 218.

(17) W. J. Gensler, E. M. Behrmann, and G. R. Thomas, *J. Am. Chem. Soc.*, **73**, 1071 (1951).

(18) W. G. Brown, *Org. Reactions*, **6**, 469 (1951).

(19) C. Collaud, *Helv. Chim. Acta*, **26**, 1064 (1943).

(20) G. H. Jeffrey and A. I. Vogel, *J. Chem. Soc.*, 674 (1948).

(21) J. Cason and F. S. Prout, *J. Am. Chem. Soc.*, **66**, 48 (1944).

(22) See ref. 14, p. 219.

B. **In the Presence of Hydrazine Hydrate.**—The procedure was essentially the same as above, except for the addition of 22 ml. of 80% hydrazine hydrate. The reaction product (7.8 g. which was distilled at 135–170° at 3 mm.) deposited 1.8 g. of solid substance identified as 10-ketoundecanoic acid by mixture melting point. The liquid fraction (6.0 g.) gave the *p*-bromophenacyl ester, m.p. 68.0–68.5°, which did not depress the melting point when admixed with an authentic sample of *p*-bromophenacyl undecanoate, m.p. 68.0–68.9° (lit.[23] m.p. 69°).

cis-**15-Heptadecenoic Acid.**—The preparative method of 15-heptadecenoic acid from 15-heptadecenoic acid[1] was similar to that adopted in the preparation of VIII; thus, 11.0 g. of 15-heptadecenoic acid was converted to 10.5 g. (96%) of crude 15-heptadecynoic acid, m.p. 72–74°, which was recrystallized from *n*-pentane. The pure sample melted at 77.4–77.7° and depressed the melting point when admixed with VIII.

Anal. Calcd. for $C_{17}H_{30}O_2$: C, 76.68, H, 11.35. Found: C, 76.87; H, 11.43.

The *p*-bromophenacyl ester was prepared in the usual manner[24] and melted at 79.5–80.0° after recrystallizations from ethanol.

Anal. Calcd. for $C_{25}H_{35}BrO_3$: C, 64.79; H, 7.61. Found: C, 64.88; H, 7.66.

A sample of 15-heptadecynoic acid (1.76 g.) in a mixed solvent composed of 30 ml. of methanol and 50 ml. of ethanol was hydrogenated at atmospheric pressure over Lindlar catalyst.[10] After 188 ml. (calculated 161 ml.) of hydrogen was absorbed, usual work-up gave 1.68 g. of wax-like substance, m.p. 43–45°, which melted at 44.0–45.0° after two recrystallizations from *n*-hexane, ν_{max} (Nujol) 960 cm.$^{-1}$ (trace).

Anal. Calcd. for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02. Found: C, 75.99; H, 12.01.

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(23) C. V. Wilson, *J. Am. Chem. Soc.*, **67**, 2162 (1945).

(24) See ref. 14, p. 200.

Direct Synthesis of Dihydrocoumarin and Its Derivatives

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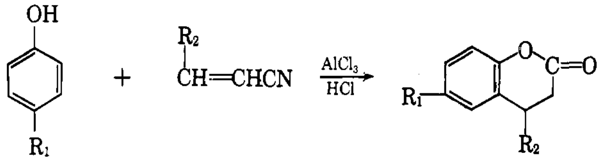
Reaction of acrylonitrile with phenol or the *para*-substituted phenols in the presence of anhydrous aluminum chloride and dry hydrogen chloride provided considerably good yields of dihydrocoumain or 6-substituted dihydrocoumarins in one step. It fails with phenols which are sufficiently deactivated by electron-attractive groups. Similarly reaction of crotononitrile with the *para*-substituted phenols gave the corresponding 4-methyldihydrocoumarin derivatives.

Dihydrocoumarins may be obtained by the catalytic hydrogenation of coumarins.[2] The carbon–carbon cyanoethylation of the more active phenols, such as resorcinol, is known to give dihydrocoumarin derivatives in the presence of anhydrous zinc chloride and dry hydrogen chloride.[3] Phenol itself does not react under these conditions, but, if a more active catalyst, anhydrous aluminium chloride, is used, a good yield of β-(*p*-hydroxyphenyl)propionitrile is obtained.[4] The addition of vinylidene cyanide to phenol in the presence of anhydrous aluminum chloride gives β-(*p*-hydroxyphenyl)-α-cyanopropionitrile and a trace of dihydrocoumarin.[5] The cyanoethylation of phenol by acrylonitrile gives β-(*p*-hydroxyphenyl)propionitrile and a small amount of dihydrocoumarin.[6] Recently Kost, *et al.*, have reported that the cyanoethylation of *p*-cresol by acrylonitrile gives β-(2-hydroxy-5-methylphenyl)propionitrile and a trace of 6-methyldihydrocoumarin.[7]

The authors have now found the following modified method of preparing dihydrocoumarins.



I II III

R_1 = –H, –CH_3, –OCH_3, –Cl
R_2 = –H, –CH_3

The reactions of nitrile II with phenol I were carried out at 120–145° in the presence of 1 mole of anhydrous aluminium chloride per mole of phenol I and an excess of dry hydrogen chloride. The data, summarized in Tables I and II, indicate the scope of these procedures.

These dihydrocoumarins were identified by their infrared spectra and microanalyses. The following compounds which were sufficiently deactivated by electron-attractive groups did not react: *p*-acetylaminophenol, methyl *p*-hydroxybenzoate, *p*-hydroxyacetophenone, *p*-phenol sulfonic acid, and *p*-nitrophenol.

The reactions of crotononitrile with phenols provided poor yields of 4-methyldihydrocoumarins. No *para* addition product was isolated from the reaction of crotononitrile with phenol. It was very difficult to isolate 4-methyldihydrocoumarins from crude products by repeated refractionation. This is probably because 4-methyldihydrocoumarins formed azeotropes with crotonamide. It was possible to isolate the pure products by gas chromatographing over silicon oil (D. C. 550).

Although several experiments were made under the described conditions, the reaction with crotononitrile produced a lower yield than with acrylonitrile. This result suggests the influence of steric hindrance and hyperconjugation.

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(1) On leave of absence from the Seimi Chemical Laboratory, Chigasaki, Japan, 1962–.

(2) P. L. De Benneville and R. Conner, *J. Am. Chem. Soc.*, **62**, 283 (1940); L. Palfray, *Bull. Soc. Chim.*, **7**, 401 (1940); C. L. Palfray, *J. Am. Chem. Soc.*, **63**, 3540 (1941); Y. Ito, H. Kitagawa, T. Hiramori, Y. Suzuki, and M. Yamagata, *J. Pharm. Soc. Japan*, **71**, 686 (1951); Y. Ito and H. Kitagawa, *J. Pharm. Soc. Japan*, **73**, 107 (1953); P. Maitte, *Ann. chim.* (Paris), **9**, 431 (1954); T. R. Ingle and B. V. Bride, *J. Univ. Bombay*, **23** [Pt. 3], *Sect. A*, No. 36, 33 (1954); F. Korte and K. H. Bückel, *Chem. Ber.*, **93**, 1025 (1960).

(3) W. D. Langley and R. Adams, *J. Am. Chem. Soc.*, **44**, 2320 (1922); E. Chapman and H. Stephen, *J. Chem. Soc.*, **127**, 885 (1925).

(4) (a) R. Schnabel, German Patent 870,273 (1953); (b) C. Bayer, *Angew. Chem.*, **61**, 239 (1949).

(5) J. C. Westfahl and T. L. Greham, *J. Am. Chem. Soc.*, **76**, 1076 (1954).

(6) H. W. Johnston and F. J. Gross, *J. Org. Chem.*, **22**, 1264 (1957).

(7) A. N. Kost, B. M. Kost, B. M. Sheiman, and A. P. Terent'er, *Zh. Obshchei. Khim.*, **29**, 2310 (1959); B. M. Sheiman and A. N. Kost, *Vestnik. Moskov. Univ., Ser. II*, **15**, [5], 65 (1960).