tion obtained in this work had the constants, b. p. 109° (65 mm.), $n^{20}_D$ 1.4269. A 2,4-dinitrophenylhydrazone was prepared which had a constant melting point of 111–112° after two recrystallizations from ethanol.

*Anal.* Calcd. for $C_{16}H_{22}O_4N_4$: C, 55.88; H, 6.88. Found: C, 55.80; H, 6.90.

## Summary

2-Ethyl-, 2-isopropyl- and 2-*n*-amyl-1,3-butadiene have been prepared by a general procedure which can presumably be applied to other 2-alkylbutadienes.

Experiments covering alternate routes to various of the intermediates and final products have been recorded.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF AGRICULTURE, UNIVERSITY OF WISCONSIN]

# The Synthesis of Unsaturated Fatty Acids[1]

BY KAMALLUDIN AHMAD AND F. M. STRONG

Despite the large number of unsaturated fatty acids which occur in the most diverse types of living organisms and their great technical and biological importance, only a very few have been synthesized to date by methods which could be expected to lead to pure products of unequivocal structure.[2] Recent improvements in methods for selectively hydrogenating acetylenes to olefins[3,4,5] and the ease of building up relatively long aliphatic chains by condensing alkyl halides with acetylene or alkyl acetylenes[6] suggested the possibility of obtaining unsaturated fatty acids from acetylenic alkyl halides *via* the nitrile or Grignard reagent:

$$\mathrm{R{-}C{\equiv}C{-}(CH_2)_nX \longrightarrow R{-}C{\equiv}C(CH_2)_n{-}COOH \longrightarrow R{-}CH{=}CH{-}(CH_2)_n{-}COOH}$$

It was expected that acetylenic halides of the required type would be formed by reaction of alkyl acetylenes with, for example, bromo- or iodochlorides since acetylene itself readily yields analogous products.[7]

$$\mathrm{RC{\equiv}CH + I(CH_2)_n{-}Cl \xrightarrow{NaNH_2} RC{\equiv}C{-}(CH_2)_nCl}$$

The feasibility of this method of synthesis has been tested by the preparation of 6-hendecenoic acid from 1-hexyne and 1-chloro-4-iodobutane according to the scheme

$$\mathrm{CH_3(CH_2)_3{-}C{\equiv}CH + I(CH_2)_4Cl \xrightarrow{NaNH_2} CH_3(CH_2)_3C{\equiv}C{-}(CH_2)_4Cl \xrightarrow[NaOH]{NaCN} CH_3(CH_2)_3C{\equiv}C{-}(CH_2)_4COOH \xrightarrow[Ni]{(H)} CH_3(CH_2)_3CH{=}CH(CH_2)_4COOH}$$

The desired product was obtained with no particular difficulty, and the olefinic bond was found by oxidative degradation to be present in the expected position.

## Experimental

**1-Chloro-4-iodobutane.**—Sodium iodide was refluxed in acetone solution with a three-molar proportion of 1,4-dichlorobutane[8] until less than 3% of the iodine remained in the inorganic form (five to six hours). Fractional distillation gave a 71% yield (based on the sodium iodide) of 1-chloro-4-iodobutane, b. p. 93–94.5° (17 mm.), of 94% purity.

*Anal.* Calcd. for $C_4H_8ClI$: I, 58.1. Found: I, 54.4.

Since the impurity was most probably unreacted dichlorobutane, the product was used without further purification.

**1-Chloro-5-decyne.**—A three-liter, three-neck round-bottom flask was fitted with a stirrer, dropping funnel, gas inlet tube, and block tin condenser cooled with a chloroform–Dry Ice mixture. Fifteen-hundred ml. of liquid ammonia was placed in the flask, the stirrer was started, and 0.3 g. of ferric nitrate and 1 g. of sodium were added. Dry air was bubbled through the solution for a few minutes until the blue color was discharged, after which an additional amount of 14.6 g. (0.68 g. atom, total) of sodium was added slowly in small portions. After the reaction had been in progress for thirty minutes, 1 g. of sodium peroxide was added. After two and one-half hours the mixture assumed a dull gray color, and the conversion of the sodium to sodamide was judged to be complete.[9]

An amount of 41 g. (0.50 mole) of 1-hexyne[10] was then introduced dropwise with stirring over a period of two hours, and after an additional interval of three hours, 117 g. (0.54 mole) of 1-chloro-4-iodobutane was added during four hours. Stirring was continued four hours longer, and the mixture was then allowed to stand at room temperature until the ammonia had evaporated. About 150 ml. of water was cautiously added, the mixture filtered, and the organic layer collected in ether. The ether solution was washed free from inorganic halides with water, and fractionally distilled. The main fraction, 45.4 g. (53%), b. p. 143–145° (51 mm.), contained 2.5% of iodine. Redistillation gave 31 g. of iodine-free product, b. p. 110–112° (15 mm.); $n^{25}_D$ 1.4592, $d^{25}_4$ 0.9238, *MR* (calcd.) 51.4, *MR* (found) 51.1. The yield of pure product thus amounted to 36%.

*Anal.* Calcd. for $C_{10}H_{17}Cl$: Cl, 20.53. Found: Cl, 19.6, 20.6.

**6-Hendecynoic Acid.**—To a solution of 16 g. (0.33 mole) of sodium cyanide in 25 ml. of water were added 115 ml. of 95% ethanol and 25.7 g. (0.15 mole) of 1-chloro-5-decyne. The mixture was refluxed until the bulk of the chloride had been converted to the inorganic

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(1) Published with the approval of the Director of the Wisconsin Agricultural Experiment Station.

(2) K. S. Markley, "Fatty Acids," Interscience Publishers, Inc., New York, N. Y., 1947, p. 554.

(3) Campbell and Eby, THIS JOURNAL, **63**, 2683 (1941).

(4) Thompson and Shaw, *ibid.*, **64**, 363 (1942).

(5) H. Adkins, private communication.

(6) Vaughn, Hennion, Vogt and Nieuwland, *J. Org. Chem.*, **2**, 1 (1937).

(7) Henne and Greenlee, THIS JOURNAL, **67**, 484 (1945).

(8) E. I. du Pont de Nemours and Company, Electrochemical Division, generously donated this material.

(9) Vaughn, Vogt and Nieuwland, THIS JOURNAL, **56**, 2120 (1934).

(10) Farachan Laboratories, Cleveland, Ohio.

form (fifteen hours), after which 20 g. of sodium hydroxide was added and the refluxing continued overnight. Most of the alcohol was then distilled off, water added, and the alkaline solution extracted with ether. Acidification of the aqueous solution caused the separation of an oily liquid which was collected in ether, and fractionated to give 19 g. of material b. p. 126–150° (0.5 mm.). Since the neutral equivalent was high, the entire fraction was again dissolved in aqueous alkali and extracted with ether to remove neutral impurities. Isolation of the acid fraction as before, followed by distillation gave 10.4 g. (38%), b. p. 124–125° (0.17 mm.); $n^{25}{}_D$ 1.4566, $d^{25}{}_4$ 0.9537, *MR* (calcd.) 52.5, *MR* (found) 52.1.

*Anal.* Calcd. for $C_{11}H_{18}O_2$: C, 72.47; H, 9.96; neutral equivalent, 182.3. Found: C, 72.1; H, 9.98; neutral equivalent, 181.5, 182.0.

Quantitative microhydrogenation showed an uptake of 1.98 moles of hydrogen per mole of compound. Calculated, 2.00 moles. The *p*-phenyl phenacyl ester was prepared according to the directions given by Price and Griffith,[11] and after recrystallization from 65% ethanol melted at 58°.

*Anal.* Calcd. for $C_{25}H_{28}O_3$: C, 79.75; H, 7.49. Found: C, 79.78; H, 7.00.

**Hendecanoic Acid.**—An amount of 0.9774 g. of the above 6-hendecynoic acid was dissolved in 15 ml. of alcohol, and shaken at room temperature in an atmosphere of hydrogen with 59.8 mg. of platinum oxide catalyst. Absorption of the theoretical amount of hydrogen was complete in fifteen minutes. The catalyst and solvent were removed, and the product crystallized from a small volume of acetone. Colorless crystals, m. p. 28°, were obtained. The m. p. of hendecanoic acid has been reported to be 28.8–29.2°.[12]

*Anal.* Calcd. for $C_{11}H_{22}O_2$: neutral equivalent, 186.3. Found: neutral equivalent, 186.2, 186.0.

A small sample was converted to the *p*-phenyl phenacyl ester, which was recrystallized from 65% alcohol, and melted at 79.5°. The literature value is 79.5–80°.[11]

**6-Hendecenoic Acid.**—An alcoholic solution of 4.8 g. of 6-hendecynoic acid was shaken under approximately 3 atmospheres pressure of hydrogen in the presence of Raney W6 nickel catalyst.[13] One molar equivalent of hydrogen was absorbed in a few minutes, and the reduction was then immediately stopped. After removing the catalyst and solvent the product was distilled, and yielded 3.00 g. (62%) of a colorless liquid, b. p. 130–134° (0.15 mm.); $n^{25}{}_D$ 1.4492, $d^{25}{}_4$ 0.9208, *MR* (calcd.) 54.1, *MR* (found) 53.7.

*Anal.* Calcd. for $C_{11}H_{20}O_2$: C, 71.68; H, 10.91; neutral equivalent, 184.3. Found: C, 71.3; H, 10.69; neutral equivalent, 185.0.

Quantitative microhydrogenation resulted in the absorption of 0.97 mole of hydrogen per mole of the compound; calculated, 1.00 mole.

The *p*-phenyl phenacyl ester was prepared in the usual way and melted at 41°.

*Anal.* Calcd. for $C_{25}H_{30}O_3$: C, 79.33; H, 8.04. Found: C, 79.2; H, 8.10.

**Oxidative Degradation of 6-Hendecenoic Acid.**—One gram of 6-hendecenoic acid was oxidized with dilute alkaline permanganate by the procedure of Lapworth and Mottram.[14] Since the expected dihydroxy acid did not precipitate on acidification of the reaction mixture, the acidic solution was thoroughly extracted with ether. Removal of the ether followed by extraction of the residue with petroleum ether and drying gave 0.31 g. of the crude dihydroxy acid, which was not further purified.

The acidic aqueous solution and petroleum ether washings were combined, evaporated to dryness under reduced pressure, and the residue taken up in absolute alcohol. The solution was neutralized with sodium hydroxide, and the acid present converted to the *p*-phenyl phenacyl ester in the usual way. The recrystallized product melted at 146°. The *bis-p*-phenyl phenacyl ester of adipic acid is reported to melt at 148°.[15] A mixed melting point with an authentic specimen showed no depression.

The crude dihydroxy acid (0.31 g.) was dissolved in 5 ml. of anhydrous acetic acid and treated with 0.45 g. of lead tetraacetate. After shaking for twenty minutes at room temperature and five minutes at 45°, the mixture was cooled, diluted with 5 ml. of water, and 0.3 g. of hydroxylamine hydrochloride, 0.3 g. of sodium acetate, and 3–4 drops of methanol were added. The crystals which separated on standing overnight at 7° were filtered, washed with cold, dilute sodium hydroxide solution, then with water and dried. The product melted at 51°. *n*-Valeraldehyde oxime melts at 52°.[16] A mixed melting point with an authentic specimen showed no depression.

## Discussion

Suitable selection of the intermediate halides should permit extension of the present synthesis to a wide variety of saturated, olefinic and acetylenic straight and branched chain acids, while reaction of the intermediate acetylenes with aldehydes, ketones or acid halides should result in hydroxy or keto derivatives. A series of straight chain, mono-unsaturated acids is being prepared in this Laboratory.

No effort was made to isolate the two geometrical isomers of 6-hendecenic acid. However, the present synthesis should offer opportunities for obtaining such isomers, since the partial hydrogenation of the acetylenic bond can be stereochemically controlled.[17]

## Summary

A convenient and practical synthesis of mono-unsaturated fatty acids has been suggested. Alkyl acetylenes react with iodochlorides to form acetylenic chlorides which in turn, *via* the nitrile or Grignard reaction and subsequent selective hydrogenation of the triple bond, are converted to the mono-unsaturated fatty acids. The method promises to be of general utility for synthesizing a variety of fatty acids and related long chain aliphatic substances.

MADISON, WISCONSIN RECEIVED NOVEMBER 17, 1947

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[11] Price and Griffith, THIS JOURNAL, **62**, 2884 (1940).

[12] Kulka and Sandin, *ibid.*, **59**, 1347 (1937).

[13] Adkins and Billica, *ibid.*, **70**, 695 (1948).

[14] Lapworth and Mottram, *J. Chem. Soc.*, **127**, 1628 (1925).

[15] Drake and Sweeney, THIS JOURNAL, **54**, 2060 (1932).

[16] Huntress and Mulliken, "Identification of Pure Organic Compounds, Order 1," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 51.

[17] Campbell and Eby, THIS JOURNAL, **63**, 216 (1941).