cyanocrotonate cannot account for the production of intermediates II and III and the end product IV, it is obvious that 1,4-addition leading to I took place as expected. This addition product I should be especially useful as a starting material in the preparation of α-substituted allenolic acids (under investigation).

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Experimental[6]

Preparation of Starting Materials.—The 2-bromo-6-methoxynaphthalene was prepared by bromination of β-naphthol followed by reduction with tin and hydrochloric acid according to Koelsch.[7] Methylation and conversion to the Grignard reagent were carried out as described in the literature.[8] The methyl α-cyanocrotonate was prepared from acetaldehyde and cyanoacetic acid according to Young and co-workers.[9]

α-Carboxy-β-(6-methoxy-2-naphthyl)-butyramide (II).—A solution of 6-methoxy-2-naphthylmagnesium bromide was prepared from 1.07 g. of magnesium, 6.40 g. of 6-methoxy-2-bromonaphthalene and 1.0 g. of ethyl bromide in 50 ml. of a 3:5 mixture of ether–benzene. The dark brown solution was cooled to 5° and treated dropwise while stirring with a solution of 5.60 g. of methyl α-cyanocrotonate in 25 ml. of ether over a period of 20 min. The mixture was hydrolyzed with dilute sulfuric acid and more ether added. After two water-washes, the ether–benzene phase was dried and evaporated to yield an oil which was distilled *in vacuo*. A volatile fraction, b.p. 80–90° (0.1 mm.), was discarded and a sirupy fraction, b.p. 200–210° (0.1 mm.), consisting of methyl α-cyano-β-(6-methoxy-2-naphthyl)-butyrate (I) weighed 4.30 g. (56% yield).

This oil was dissolved in 25 ml. of methanol and 5 ml. of a 70% aqueous sodium hydroxide solution added. The mixture was heated under reflux for 4 hours after which time a considerable precipitate was collected by filtration. It was dissolved in 200 ml. of water and the solution after one ether-wash was acidified to liberate 1.80 g. (40% yield based on I) of needles m.p. 135–140° dec. Four recrystallizations from methanol afforded colorless prisms of α-carboxy-β-(6-methoxy-2-naphthyl)-butyramide (II) m.p. 138–139° dec.

Anal. Calcd. for $C_{16}H_{17}O_4N$: C, 66.89; H, 5.92; N, 4.87; neut. equiv., 287. Found: C, 66.52; H, 6.20; N, 4.85; neut. equiv., 287.

β-(6-Methoxy-2-naphthyl)-butyramide (III).—Of the above α-carboxy-β-methyl-6-methoxy-2-naphthalenepropionamide, 500 mg. was heated to 150° in an oil-bath until gas evolution had ceased. Upon cooling, the melt solidified and was recrystallized from methanol to yield 414 mg. (98% yield) of colorless prisms, m.p. 173–173.5°.

Anal. Calcd. for $C_{15}H_{17}O_2N$: C, 74.07; H, 6.99; N, 5.76. Found: C, 73.95; H, 6.74; N, 5.75.

β-(6-Methoxy-2-naphthyl)-butyric Acid (IV).—Twenty-five milligrams of the preceding β-methyl-6-methoxy-2-naphthalenepropionamide was dissolved in 10 ml. of 5% methanolic potassium hydroxide and the solution heated under reflux for 3 hours after which time it was poured into 50 ml. of water. After one ether-wash, the solution was acidified and extracted with ether. The ether was dried and evaporated to yield 23 mg. (92% yield) of material, m.p. 131–133°. Two recrystallizations from aqueous methanol afforded colorless needles, m.p. 133–133.5°.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.77; H, 6.55; neut. equiv., 244. Found: C, 73.30; H, 6.76; neut. equiv., 244.

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(6) Melting points and boiling points are uncorrected and Mr. Y. Perron of University of Montreal kindly performed the microanalyses.

(7) C. F. Koelsch, *Org. Syntheses*, **20**, 29 (1940).

(8) K. Fries and K. Schimmelschmidt, *Ber.*, **58**, 2840 (1925).

(9) W. G. Young, L. J. Andrews, S. L. Lindenbaum and S. J. Cristol, THIS JOURNAL, **66**, 811 (1944).

Action of Lithium Aluminum Hydride on Acetylenic Acids

BY GLEN E. BENEDICT AND ROBERT R. RUSSELL

A study of the reduction of acetylenic acids with lithium aluminum hydride has been made during an investigation of a radio-carbon synthesis procedure. In an effort to reduce the number of steps in this procedure an attempt was made to reduce triple bond acids to double bond alcohols. The method used was essentially that of Nystrom and Brown[1] with the exception that the acids were left in contact with the ether solution of lithium aluminum hydride twice as long.

The acids used in this study were acetylenedicarboxylic and propiolic. Reductions were also carried out on fumaric and acrylic acids to check product behavior and the previously reported conclusions that aliphatic double bond acids were reduced to the corresponding double bond alcohols. All acids used were soluble except fumaric which was extracted into the reaction flask from a Soxhlet thimble.

The results of this investigation indicate the triple bond acids used were reduced and hydrogenated by the action of a 25% excess of lithium aluminum hydride at room temperature to the double bond alcohols.

All product alcohols decolorized bromine rapidly. The phenyl isocyanate derivatives of the reduction products from propiolic and acrylic acids showed no melting point depression when mixed with an authentic sample prepared from allyl alcohol.

A sample of the reduction product of acetylenedicarboxylic acid was titrated with a bromine in chloroform solution and the results indicated the formation of 2-butene-1,4-diol of 98% purity. The ethyl chlorocarbonate derivatives of the diols were prepared, melting points were taken for each separately and mixed. These corresponded closely and the mixed solid showed no tendency to melt lower than either alone.

Experimental

Reduction of Acetylenedicarboxylic Acid.—In a typical reaction 750 ml. of anhydrous ether was placed in a 2-liter, three-necked flask filled with a mechanical stirrer, dropping funnel and drying tube equipped condenser. An atmosphere of dry nitrogen was provided and 0.5 mole (19.5 g.) of lithium aluminum hydride was dissolved in the ether solution by stirring for three hours. When solution was complete 250 ml. of ether containing 0.2 mole (22.8 g.) of acetylenedicarboxylic acid was added dropwise and the resultant mixture stirred at room temperature for 16 hours. The excess hydride was then cautiously decomposed with water and the lithium aluminum organo intermediate was decomposed with 20% sulfuric acid. The two layers were separated and the aqueous layer was continuously extracted with ether. Ferrous ion was added to the water solution to decompose ether peroxide, so easily formed during continuous extraction operations. After drying with anhydrous sodium sulfate and treatment with potassium carbonate to remove any unreacted acid, the ether was removed by distillation. The residual 2-butene-1,4-diol, 15.7 g. (84%) was a liquid boiling at 128–130°. The purified product formed an oily granular mass when cooled in the ice-bath melting at room temperature.[2]

The **ethyl chlorocarbonate** derivative of the 2-butene-1,4-diol was prepared from 0.2 g. of alcohol 0.4 g. of pyridine in

(1) R. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 2548 (1947).

(2) W. E. Bissinger, *ibid.*, **69**, 2957 (1947), has reported the melting point of 2-butene-1,4-diol as 25°.

2 ml. of ether cooling to −4° and adding 0.5 g. of ethyl chlorocarbonate. The solid (m.p. 94.6–97°) decomposed upon standing. Mixed melting point determinations showed it to be identical with the derivative prepared from the reduction of fumaric acid.

Reduction of Fumaric Acid.—In a manner similar to the above, 0.2 mole of fumaric acid was reduced with 0.5 mole of lithium aluminum hydride to 2-butene-1,4-diol in 78% yield. Titration of a sample of the product with bromine in chloroform indicated that the unsaturated diol was 98.1% pure.

Reduction of acrylic acid was also carried out as in the previously described reactions. The yield of allyl alcohol (68.3%) was obtained from 0.283 mole of acid and 0.35 mole of the hydride. The derivative of the alcohol (m.p. 67.8–68.6°) prepared by treatment with phenyl isocyanate was shown by mixed melting point determination to be identical with an authentic sample.

Reduction of Propiolic Acid.—The reduction of the triple bond acid was carried out as described above, using 0.285 mole of acid and 0.35 mole of lithium aluminum hydride. Allyl alcohol was produced in 85% yield as an azeotrope boiling at 78–81°. Mixed melting point determinations of the phenylurethan derivative showed no depression when mixed with an authentic sample.

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The Rate of Reaction of Cyclopentyl Chloride with Potassium Iodide in Acetone[1]

BY F. G. BORDWELL AND GLENN D. COOPER

In a recent investigation of the reduction of sulfones by lithium aluminum hydride,[2] it was observed that five-membered ring sulfones are reduced at a much faster rate than open-chain sulfones. One possible formulation of this reaction is displacement of the oxygen by attack of aluminohydride ion (AlH_4^-) on sulfur. It, therefore, seemed worthwhile to determine whether or not cyclopentyl halides showed enhanced reactivity as compared to open-chain secondary halides in displacement reactions. The remarkable inertness of cyclohexyl halides and the current interest in the effect of ring size on halide reactivity[3] afforded additional incentives.

Cyclopentyl bromide reacts readily with sodium iodide in acetone,[4a] and with a variety of other nucleophilic reagents,[4b] but the rates of these reactions have not been measured. Accordingly, the rate of reaction of cyclopentyl chloride with potassium iodide in acetone at 58.5° was determined; $k_{58.5°} = 7.0 \times 10^{-3}$ liter mole^{-1} hr.$^{-1}$. The rates of this reaction for five methylalkylcarbinyl chlorides were reported by Conant and Hussey[5]; the k values obtained at 60° ranged between 3.4×10^{-3} and 17.2×10^{-3}.[6] It is apparent that the rate of reaction of cyclopentyl chloride with potassium iodide in acetone is comparable with that of open-chain secondary chlorides.

Experimental

The rates were measured by the method of Conant and Kirner.[7] Cyclopentyl chloride was prepared from cyclopentanol and concentrated hydrochloric acid; b.p. 111° (750 mm.), $n^{20}D$ 1.4500; literature[4a] b.p. 111–112°, $n^{25}D$ 1.4485.

Rate at $t = 58.5 \pm 0.05°$

Time, hr.	Reacted, %	$k \times 10^3$
72	9.6	7.1
120	16.1	7.0
236	27.2	6.8
	Average	7.0

The solution was only very faintly colored by iodine after 236 hours.

The rate of reaction of isopropyl chloride, measured for comparison, was $k_{58.5°} = 2.8 \times 10^{-3}$; Conant and Hussey[5,6] obtained $k_{60°} = 3.4 \times 10^{-3}$.

(1) This investigation was supported by the Office of Naval Research under Contract No. N7onr-45007.

(2) Bordwell and McKellin, THIS JOURNAL, **73**, 2251 (1951).

(3) Brown, Fletcher and Johannesen, *ibid.*, **73**, 212 (1951).

(4) (a) Rogers and Roberts, *ibid.*, **68**, 843 (1946); (b) Loevenich, Utsch, Moldrickx and Schaefer, *Ber.*, **62B**, 3084 (1929).

(5) Conant and Hussey, THIS JOURNAL, **47**, 476 (1925).

(6) These are values of k. The values reported by Conant and Hussey are for $0.4343k$.

(7) Conant and Kirner, THIS JOURNAL, **46**, 232 (1924).

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Fluoroacetylcholine Bromide and Some Other Choline Ester Salts

BY THOMAS R. BLOHM

The striking differences between the parasympathomimetic activities of acetylcholine and its chloro-[1] and bromo-substitution[2] products could be due either to the electronegative character of these halogens, or the size of their atoms compared to hydrogen. Since fluorine more nearly approaches hydrogen in size while retaining high electronegativity, it was thought to be of interest to prepare fluoroacetylcholine. Interest in this compound also stems from the ability of fluoroacetic acid to block the Krebs cycle.[3]

In addition to fluoroacetylcholine bromide, the syntheses of trichloroacetylcholine perchlorate, dichloroacetylcholine perchlorate, fluoroacetylcholine perchlorate and β-bromoethyl fluoroacetate are described.

Preliminary pharmacological data on rabbits indicate that these choline esters are much less active than acetylcholine in their parasympathomimetic effects when given by the intravenous route.

Experimental

Fluoroacetyl Chloride.—This intermediate was prepared by the method of Gryskiewicz-Trochimowski, Sporzynski and Wnuk[4] using fluoroacetic acid, benzotrichloride and zinc chloride. This method was found to be definitely superior to methods using phosphorus pentachloride, inasmuch as preparations made with this reagent were found to contain phosphate—yielding contaminants even after careful fractionation. Fluoroacetic acid was prepared from the sodium salt (90%, Monsanto) and 100% H_2SO_4, similarly to the procedure of Saunders and Stacey.[5]

β-Bromoethyl Fluoroacetate.—Five grams (0.040 mole) of freshly distilled ethylene bromohydrin was dissolved in 25 ml. of dry benzene and added to 5.0 g. (0.052 mole) of fluoroacetyl chloride, also dissolved in 25 ml. of dry benzene in a 100-ml. round-bottomed flask. The mixture was refluxed on a boiling water-bath for one hour; the benzene

(1) R. R. Renshaw and J. C. Ware, THIS JOURNAL, **47**, 2989 (1925).

(2) D. Glick, *J. Biol. Chem.*, **130**, 530 (1939).

(3) G. R. Bartlett and E. S. G. Barron, *ibid.*, **170**, 67 (1947); G. Kalnitsky and E. S. G. Barron, *Arch. Biochem.*, **19**, 75 (1948); W. B. Elliott and G. Kalnitsky, *J. Biol. Chem.*, **186**, 487 (1950).

(4) Gryskiewicz-Trochimowski, Sporzynski and Wnuk, *Rec. trav. chim.*, **66**, 413 (1947).

(5) B. C. Saunders and G. V. Stacey, *J. Chem. Soc.*, **58**, 1777 (1948).