

## THE SYNTHESIS AND REDUCTION OF SOME POLYFUNCTIONAL ACETYLENIC COMPOUNDS

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In connection with studies on possible synthetic routes to Vitamin A methyl ether, we studied the partial hydrogenation of certain polyfunctional acetylenic compounds. Herein we report some of the more interesting facts.

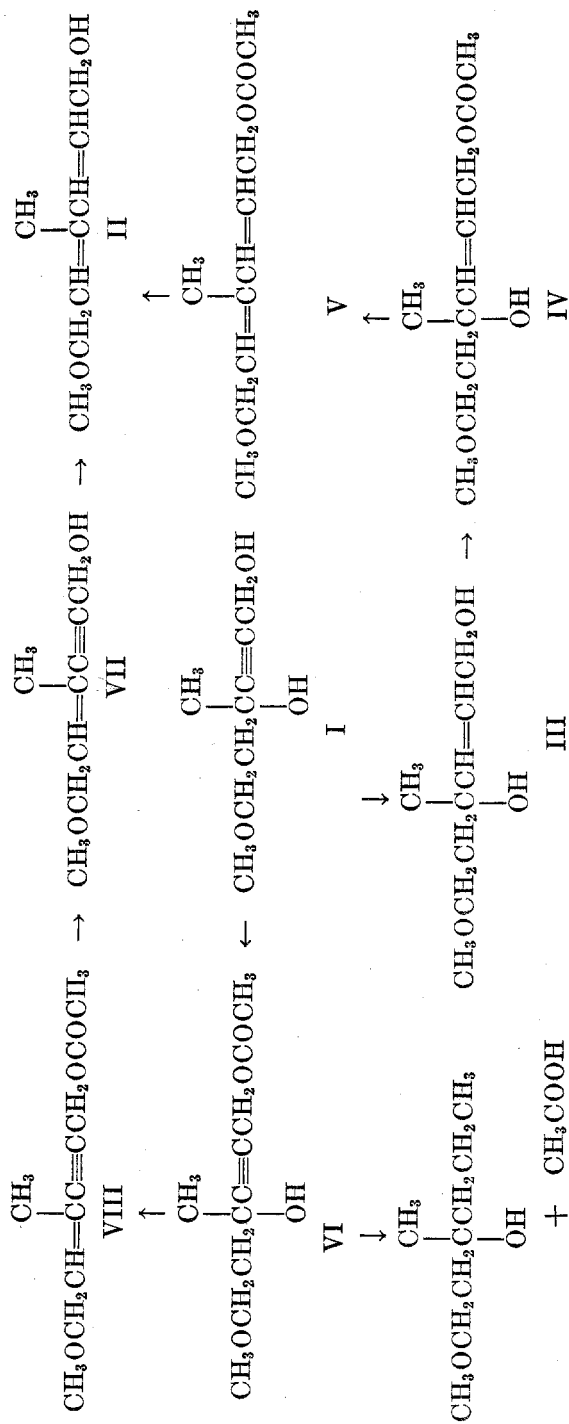
One problem involved the conversion of 6-methoxy-4-methyl-2-hexyn-1,4-diol<sup>2</sup> (I) into 6-methoxy-4-methyl-2,4-hexadiene-1-ol (II). For this purpose two goals had to be achieved: the reduction of the triple to a double bond; and selective removal of the tertiary hydroxyl by dehydration. To accomplish the latter it was thought desirable to protect the primary hydroxyl by acetylation but it was not known whether the selective hydrogenation of the triple bond should be carried out before or after dehydration or before or after acetylation of the primary hydroxyl. As a result of experiments which tested each of the possible routes (see chart) the following scheme was found best; reduction of I to 6-methoxy-4-methyl-2-hexen-1,4-diol (III); acetylation to the corresponding primary acetate, IV; dehydration to the acetate of 6-methoxy-4-methyl-2,4-hexadien-1-ol (V); and alcoholysis to the desired II (see reaction scheme).

Hydrogenation studies were carried out with Adams platonic oxide catalyst and with a 20% palladium-on-charcoal catalyst (1). The latter proved preferable for selective hydrogenation and most of the results described were obtained with this catalyst. The hydrogenation of I proceeded smoothly until one equivalent of hydrogen had been absorbed whereupon there was a very marked decrease in hydrogen uptake. If the reaction were then stopped a good yield of III was obtained. No attempt was made to ascertain whether the product was *cis* or *trans* but in all probability it was mainly *cis*. However, when the acetate, 1-acetoxy-6-methoxy-4-methyl-2-hexyn-4-ol (VI) was reduced, considerable hydrogenolysis to yield acetic acid and ultimately 1-methoxy-3-methyl-3-hexanol occurred.

The hydrogenation of 6-methoxy-4-methyl-4-hexen-2-yn-1-ol, VII, was unusual in that even though the rate increased after one equivalent of hydrogen had been absorbed it was possible to obtain a good yield of 6-methoxy-4-methyl-2,4-hexadien-1-ol (II). This can be rationalized by assuming that the eneyne, VII, is absorbed on the catalyst much more strongly than the diene, II, so that reduction of the latter can commence only after the eneyne, VII, has been reduced, the rate of reduction of the diene being faster than that of VII (1d). This result was checked with several different preparations of VII. The reduction

<sup>1</sup> Taken in part from the Ph.D. theses of I. W. (1947) and H. G. (1947), Ohio State University.

<sup>2</sup> Since this work was completed this compound has been mentioned in British Patent 626,392.



of VIII (the acetate of VII) involved hydrogenolysis to yield acetic acid and was not studied in detail. Since propargyl acetate likewise formed acetic acid on hydrogenation it would appear that hydrogenolysis of a primary acetoxy group adjacent to a triple bond is general, (See 1c). A primary acetoxy group on the carbon *beta* to a triple bond (see 4-acetoxy-1-butyne) was not hydrogenolyzed.

4-(1-Hydroxy-1-cyclohexyl)-3-butyne-2-one (IX) would not reduce over the platinum or palladium catalysts. This was not due to a poison since the reduction of another compound could be carried out in the presence of IX. The dehydration product, 4-(1-cyclohexen-1-yl)-3-butyne-2-one (XI), of IX was reduced over both catalysts. Another fact of interest is that 2,2,6-trimethyl-1-hydroxy-1-cyclohexylpropionic acid (XII) decarboxylated in the presence of the catalysts whereas the ethyl (and methyl) ester, XIII, could be selectively reduced to the lactone of  $\beta$ -(1-hydroxy-2,2,6-trimethyl-1-cyclohexyl)acrylic acid. The decarboxylation is not general for acetylenic acids since 2-hexynoic acid (XIV) and a number of octynoic acids (2) are smoothly reduced. In an attempt to reduce XII with sodium in liquid ammonia (3) there was obtained in small yield a compound which gave analytical results consistent with its formulation as the lactone of  $\beta$ -(1-hydroxy-2,2,6-trimethyl-1-cyclohexyl)propionic acid. If this structure was correct this represents the first case of complete reduction of the acetylenic function by sodium in liquid ammonia.

Compounds XII and XIII were studied for their possible use in the synthesis of  $\beta$ -ionone but no success in this objective was attained. However, routes stemming from the above intermediates may yet be found for we did not spend as much time in this area as might be desirable.

We would like to acknowledge with thanks the generous support of the Upjohn Company, Kalamazoo, Michigan.

## EXPERIMENTAL

### PREPARATION OF MATERIALS<sup>3</sup>

*Propargyl alcohol.* This compound was prepared as described (4) from sodium acetylide and paraformaldehyde in liquid ammonia. However, if the paraformaldehyde was carefully dried over phosphorus pentoxide (two weeks with frequent stirring) and was added to the slurry of sodium acetylide in ammonia cooled to  $-70^{\circ}$  (kept at this temperature for 12 hours and then 3 hours at reflux temperature) the yield rose to nearly 30%. Later propargyl alcohol was obtained through the generosity of the General Aniline and Film Corp., Easton, Pa. Our purest synthetic samples had b.p.  $110.2^{\circ}$  at about 750 mm.;  $n_D^{20}$  1.4322.

*6-Methoxy-4-methyl-2-hexyn-1,4-diol (I).* A solution of 62 g. (1.1 moles) of propargyl alcohol in 100 cc. of ether was added during 80 minutes to 2560 cc. of 0.86 N butylmagnesium chloride (2.2 moles) with cooling. It is important to keep the stirring vigorous and *continuous* to avoid caking of the fine suspension of insoluble complex. A Zerewitinow type experiment demonstrated that both active hydrogens of the propargyl alcohol were being replaced (methylmagnesium chloride). In one experiment (by Dr. Stanley Rolfson) the use of tetrahydrofuran as part solvent kept the complex in solution but this did not result in any improvement in yield although it did simplify the operation. When alkylmagnesium bromides were used in this step the insoluble complex proved to be too viscous to stir even after adding benzene.

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<sup>3</sup> 3-Butyn-1-ol and 2-hexynoic acid (XIV) were purchased from the Farchan Chemical Co., Cleveland, Ohio.

After stirring for 30 minutes 122 g. of 1-methoxy-3-butanone (see below) in 100 cc. of ether was added during 90 minutes. The mixture was then refluxed for 12 hours and treated with about 350 cc. of saturated ammonium chloride. The ether was decanted and the salts were rinsed with more ether. Rectification afforded 75 g. (43%) of I,<sup>4</sup> b.p. 124–130° at about 2 mm., 104–105° at 0.5 mm.,  $n_D^{20}$  1.4748.

*Anal.* Calc'd for  $C_8H_{14}O_3$ : C, 60.7; H, 8.9.

Found: C, 61.3, 61.2; H, 9.3, 9.1.

The *p*-nitrophenylurethans (5) proved to be the derivative of choice for this alcohol, I, and others closely related since other common derivatives, such as *p*-nitrobenzoates, 3,5-dinitrobenzoates, phenyl- and 1-naphthyl-urethans, did not crystallize. The *p*-nitrophenylurethan of I melted at 120.4–120.8°.

*Anal.* Calc'd for  $C_{15}H_{18}N_2O_6$ : C, 55.9; H, 5.6; N, 8.7.

Found: C, 56.0, 56.1; H, 5.8, 5.9; N, 8.7, 8.8.

*Methyl vinyl ketone* (MVK) was obtained as an azeotropic mixture with water and a little acetic acid from the du Pont Co. It was isolated by adding powdered potassium carbonate until no lumping occurred on further additions. The liquid was decanted and allowed to stand over calcium sulfate (Drierite) for several hours. The solid was removed and the residue distilled under 90 mm. pressure, the distillate being collected in a Dry Ice-acetone-cooled trap to yield colorless MVK. From 300 g. of azeotrope there was obtained 215 g. of MVK, b.p. 27–29° at 90 mm.,  $n_D^{25}$  1.4082.

The yields of 1-methoxy-3-butanone obtained by the addition of methanol to MVK in the presence of a boron fluoride-mercuric oxide catalyst (8) were erratic (0–65%). However, we found that consistently good yields could be obtained with sulfuric acid catalysis. In a typical run 250 g. of MVK (freshly prepared as described above) in 250 cc. of dry methanol was added to a stirred solution of 1 cc. of concentrated sulfuric acid in 50 cc. of methanol, the temperature being maintained below 30°. After two hours at room temperature the acid was neutralized by addition of a small excess of powdered potassium carbonate. The solids were removed and on rectification there was obtained 320 g. (88%), (other runs varied from 83–90%) of 1-methoxy-3-butanone, b.p. 62–63° at 50 mm.

#### EXPERIMENTAL REACTIONS

*1-Acetoxy-6-methoxy-4-methyl-2-hexyn-4-ol* (VI). To a cooled solution of 18.5 g. of I in 25 cc. of pyridine was added 14 g. of acetic anhydride. After 15 hours the volatile products were removed under reduced pressure and the acetate,<sup>4</sup> b.p. 105° at 1 mm.,  $n_D^{20}$  1.4601, was obtained in 94% yield as a colorless oil.

*Anal.* Calc'd for  $C_{10}H_{16}O_4$ : C, 60.0; H, 8.1.

Found: C, 60.5; H, 8.3.

On hydrogenation (see Table I) this acetate was converted into 1-methoxy-3-methyl-3-hexanol. The authentic sample of this compound, b.p. 105–112° at 65 mm.,  $n_D^{25}$  1.4261, was prepared in 55% yield by adding propylmagnesium bromide to 1-methoxy-3-butanone in ether. Comparison was effected by comparing the indices of refraction at 25°: that of the hydrogenolysis product was 1.4250; that of the synthetic, 1.4261. A solid derivative was not obtained.

*Anal.* Calc'd for  $C_8H_{16}O_2$ : C, 65.7; H, 12.3.

Found: C, 65.4, 65.4; H, 12.6, 12.2.

*6-Methoxy-4-methyl-2-hexen-1,4-diol* (III). The reduction of I proceeded most rapidly in absolute alcohol when freshly distilled I was used. It was observed that there should be no less than 2 cc. of solvent for each gram of I. For 50 g. of I about 0.2 g. of 17% palladium-on-charcoal catalyst was used, reduction requiring about 2.5–3 hours. The diol, III, was obtained as a colorless oil, b.p. 84–91° at 0.5 mm.,  $n_D^{20}$  1.4670, in 75–85% yields. This compound was usually not isolated. Instead the reduction product was preferentially acetylated immediately after removal of solvent.

<sup>4</sup> These compounds were first prepared by Dr. William S. Fones, now at the National Institutes of Health, Bethesda 14, Maryland.

The acetate, IV, b.p. 90–95° at 1 mm.,  $n_D^{20}$  1.4535, was obtained in the best yield when the reduction product was acetylated directly with acetic anhydride and pyridine (slight excess) at room temperature for 48 hours. Yields averaged 85–90% over-all.

Anal. Calc'd for  $C_{16}H_{18}O_4$ : C, 59.4; H, 9.0.

Found:<sup>5</sup> C, 59.7; H, 9.0.

The *p*-nitrophenylurethan of III melted at 114.6–115.4° and the melting point was depressed by admixture of the *p*-nitrophenylurethan of 6-methoxy-4-methyl-1,4-hexanediol (see below), m.p. 116.6–117.2°.

Anal. Calc'd for  $C_{15}H_{20}N_2O_6$ : C, 55.6; H, 6.2; N, 8.6.

Found: C, 55.3, 55.6; H, 6.4, 6.3; N, 8.6, 8.9.

*6-Methoxy-4-methyl-2,4-hexadien-1-ol* (II). A typical run involved mixing 50 g. of IV with 25 g. of freshly fused powdered potassium acid sulfate followed by heating at 120° with an oil-bath. The diene acetate, V, distilled off at 1 mm. as formed and on redistillation yielded material boiling at 65–96° at 1 mm. in 77–85% yield. When this material was rectified, two fractions were obtained, the first boiling at 65–66° at 1 mm.,  $n_D^{20}$  1.4678, and the second at 70–71° at 1 mm.,  $n_D^{20}$  1.4740. On analysis each gave values consistent with formulation as V.

Anal. Calc'd for  $C_{16}H_{18}O_3$ : C, 65.2; H, 8.7.

Found: (65–66°) C, 65.0; H, 8.7.

(70–71°) C, 64.6; H, 8.7.

The following experiment was typical of those for the removal of the acetoxy group by methanolysis. A solution of 66 g. of the above acetate (mixture of isomers) in 800 cc. of cold methanol containing the sodium methoxide from 1.5 g. of sodium was held at 0–5° for 72 hours under nitrogen. To this was added 3 g. of powdered ammonium chloride and the solvent was removed under reduced pressure. The residue was taken into ether, washed with water and a saturated salt solution, and then filtered through sodium sulfate. On rectification there was obtained 37.8 g. (73%) of colorless, II, b.p. 70–85° at 1 mm.,  $n_D^{20}$  1.4910.

Anal. Calc'd for  $C_8H_{14}O_2$ : C, 67.6; H, 9.9.

Found: C, 67.5; H, 9.9.

The *p*-nitrophenylurethan melted at 116–118°.

Anal. Calc'd for  $C_{15}H_{18}N_2O_5$ : C, 58.8; H, 5.9.

Found: C, 59.1, 58.8; H, 5.7, 5.9.

*6-Methoxy-4-methyl-4-hexen-2-yn-1-ol* (VII). Considerable work was carried out with the object of dehydrating VI to VII. In a typical experiment a mixture of 50 g. of VI with 35 g. of freshly fused powdered potassium acid sulfate was heated at 120–130° under reduced pressure (1 mm.) the eneyne being distilled as formed. The distillate was redistilled to yield 36 g. (78%) of VIII<sup>4</sup> (the acetate of VII), a colorless oil, b.p. 85–108° at 1 mm. A middle cut, b.p. 95–100° at 1 mm.,  $n_D^{20}$  1.4750, was taken on redistillation for analysis.

Anal. Calc'd for  $C_{16}H_{14}O_3$ : C, 65.9; H, 7.7.

Found: C, 66.1, 65.7; H, 8.0, 8.1.

The free alcohol was obtained by methanolysis of VIII in 65–75% yields by a process similar to that described above for V. The product, VII, was a colorless oil, b.p. 76–78° at 1 mm.,  $n_D^{20}$  1.4938.

Anal. Calc'd for  $C_8H_{12}O_2$ : C, 68.5; H, 8.6.

Found: C, 68.7, 68.7; H, 8.8, 9.0.

The *p*-nitrophenylurethan melted at 111–113°. This melting point was depressed by admixture with the *p*-nitrophenylurethan of V.

Anal. Calc'd for  $C_{15}H_{16}N_2O_5$ : C, 59.2; H, 5.3.

Found: C, 59.2, 58.9; H, 5.4, 5.5.

*1-(1'-Cyclohexenyl)-1-butyne-3-one* (XI). Ethynylcyclohexanol (X) was prepared essen-

<sup>5</sup> This analytical sample was prepared by Dr. James M. Robinson, now at Merck and Co., Rahway, New Jersey.

tially according to Campbell (7) in yields which in this laboratory have frequently been 85-90% of crystalline material. For the best conversion into 1-ethynylcyclohexene (8) 595 g. (5 moles) of purified thionyl chloride in 375 cc. of dry ether was added dropwise with vigorous stirring to 620 g. (5 moles) of X in 880 cc. of dry pyridine (over BaO) in 1 l. of dry ether at a rate designed to maintain gentle reflux. After five hours at reflux, cold water was added, then cold dilute acid to remove the pyridine. On distillation there was obtained 311 g. (59%) of colorless 1-ethynylcyclohexene, b.p. 48-52° at 18 mm.,  $n_D^{24}$  1.4932. Experiments in which 2,6-lutidine, a mixture of 2,6-lutidine and 2,4,6-collidine, or pyridine were used as bases but in which the temperature was held at or below 20° throughout afforded the eneyne in 39-44% yield.

In the best of several experiments 31.8 g. (0.3 mole) of 1-ethynylcyclohexene was treated with 0.3 mole of butylmagnesium bromide for 30 minutes. This solution was then cooled to -78° under nitrogen and 0.6 mole of Dry-Ice cooled acetic anhydride in ether was added dropwise. The mixture was then allowed to warm up to -10° and was maintained at this temperature until a Michler's ketone color test was negative (3 hours). Hydrolysis with saturated ammonium chloride solution followed by rectification of the ethereal extracts afforded 13 g. (41%) of recovered 1-ethynylcyclohexene and 25 g. (56%) of XI, b.p. 92-93° at 4 mm. (b.p. 77-78° at 2 mm., 115-117° at 11 mm.),  $n_D^{25}$  1.5268 (9). The *semicarbazone*, m.p. 132.6-133.2° (8), and the *2,4-dinitrophenylhydrazone*, (8) m.p. 150.0-150.3°, were each prepared in 90% yield.

In other runs the yield of XI never went below 40%. When purified by Girard's reagent P (10) its properties were essentially unchanged. One attempt to regenerate XI from its *semicarbazone* (11) failed. In agreement with previous findings (8) we found XI to be lachrymatory and a treacherous skin irritant.

The hydrogenation of 7.31 g. of XI in 50 cc. of ethyl alcohol over 0.5 g. of a 1% palladium-on-calcium carbonate catalyst (40 p.s.i. hydrogen pressure) was stopped after one-third of an equivalent of hydrogen had been absorbed. Distillation yielded 6.0 g. of 1-(1-cyclohexenyl)-1-buten-3-one, b.p. 67° at 2 mm. The *semicarbazone*, m. p. 135.5-136.0°, was obtained in 95% yield and its melting point was depressed by admixture with the *semicarbazone* of XI. The *2,4-dinitrophenylhydrazone*, m.p. 138.8-139.6°, was formed in 97% yield.

*Anal.* Calc'd. for  $C_{15}H_{18}N_2O_5$ : C, 58.2; H, 5.5; N, 17.0.

Found: C, 58.5, 58.6; H, 5.4, 5.2; N, 16.7, 16.8.

*1-(1-Hydroxyl-1-cyclohexyl)-1-buten-3-one* (IX). Two equivalents of butylmagnesium chloride were added to 57 g. of ethynylcyclohexanol in ether. After one hour, the mixture was cooled to -78° under nitrogen and treated slowly with 102 g. of acetic anhydride. Stirring was continued for seven hours after which the mixture was allowed to come to room temperature and then was hydrolyzed with an ammonium chloride solution. On rectification there was obtained 14 g. (15%) of the acetate of IX, b.p. 105-110° at 1 mm.,  $n_D^{20}$  1.4819.

*Anal.* Calc'd for  $C_{12}H_{16}O_3$ : C, 69.2; H, 7.7.

Found: C, 69.0; H, 7.8.

The *semicarbazone* melted at 132.4-133.0°.

*Anal.* Calc'd for  $C_{12}H_{16}N_2O_5$ : C, 58.8; H, 7.2; N, 16.0.

Found: C, 58.5; H, 7.4; N, 16.3.

Compound IX was prepared from the above acetate by allowing it to stand for 12 hours in an absolute alcohol solution containing a trace of sodium ethoxide. The product, IX, was obtained (after vacuum-distillation) as a colorless solid, m.p. 65.4-66.0° in 41% yield.

*Anal.* Calc'd for  $C_{10}H_{14}O_2$ : C, 72.3; H, 8.5.

Found: C, 72.4; H, 8.8.

*1-Hydroxy-2,2,6-trimethylcyclohexylpropionic acid* (XII). To a vigorously stirred suspension of 142 g. of commercial sodium methoxide (Mathieson) in 1500 cc. of dry benzene was added 435 g. of diethyl methylmalonate (12). The viscous mixture was refluxed for one hour after which 253 g. of 1,3-dibromopropane was added dropwise, followed by 10 g. of

powdered potassium iodide. The stirred mixture was refluxed for 5 hours. After treatment with dilute hydrochloric acid, the product, ethyl 2,2,6,6-heptanetetra-carboxylate, b.p. 164–166° at 1.5 mm., was obtained in 72% yield (13). After alkaline hydrolysis, acidification, and pyrolysis, crude 2,6-dimethylheptanedioic acid was obtained. A mixture of this acid and 8 g. of powdered barium hydroxide was heated in a bath held at 335–340° to yield pure 2,6-dimethylcyclohexanone, b.p. 172–173°,  $n_D^{25}$  1.4450 (14) in 82% yield.

To a stirred suspension of 19 g. of sodium amide in 200 cc. of dry ether (under nitrogen throughout) was added 63 g. of 2,6-dimethylcyclohexanone. After refluxing for 3 hours, 71 g. of methyl iodide in 75 cc. of ether was added at a rate sufficient to maintain vigorous refluxing. After one hour at reflux there was obtained in 93% yield (calc'd as trimethylcyclohexanone) a crude ketone mixture, b.p. 176–180°. Of the methods for isolation of pure 2,2,6-trimethylcyclohexanone tried, the following is recommended.

The dimethylcyclohexanone was largely removed by rectification in about a 15-plate column. The higher-boiling fraction (104 g.) was added to a suspension of 29 g. of sodium amide in 100 cc. of benzene. After one hour the solvent was removed under reduced pressure and the unreacted tetramethyl ketone was vacuum-distilled. Ether was added to the solid residue and ice-water was added to hydrolyze the enolate. After acidification and rectification there was obtained 50 g. of rather pure 2,2,6-trimethylcyclohexanone which formed an oxime that melted at 101–103° without purification. On recrystallization from alcohol-water it was easy to isolate oxime of m.p. 102.5–103° (15) from which pure 2,2,6-trimethylcyclohexanone,  $n_D^{20}$  1.4478, was obtained (13). This ketone was reacted with sodium acetylide in liquid ammonia in the usual way (7). The reaction was allowed to proceed for seven hours with a steady stream of acetylene passing through. After neutralizing with ammonium chloride there was obtained an 89% yield of 1-ethynyl-2,2,6-trimethylcyclohexanol, b.p. 54–56° at 1 mm.,  $n_D^{23}$  1.4778 (15, 16). Attempts at dehydration of this alcohol failed (16) probably because the hydroxyl group in the isomer obtained is *cis* to the hydrogen in the 6-position. This ethynyl alcohol was converted into XII in 73% yield (87% if allowance for recovered ethynyl alcohol is made) by carbonation of the bis-bromomagnesium derivative (17). It melted at 176.4–177.2° with decomposition (decarboxylation).

*Anal.* Calc'd for  $C_{12}H_{18}O_2$ : C, 68.6; H, 8.6; N.E., 210.

Found: C, 68.7, 68.6; H, 8.8, 8.6; N.E., 211.

*Ethyl 1-hydroxy-2,2,6-trimethylcyclohexylpropionate* (XIII). The acid, XII, was esterified with 1% alcoholic sulfuric acid using benzene and removing the water formed by the azeotropic method. The ethyl ester, XIII, b.p. 114–115° at 0.5 mm., was obtained in 70% yield.

*Anal.* Calc'd for  $C_{14}H_{22}O_3$ : C, 70.5; H, 9.3.

Found: C, 70.8, 70.7; H, 9.4, 9.3.

The *methyl ester*, b. p. 110° at 1 mm.,  $n_D^{20}$  1.4940, was obtained in 81% yield by treatment of an ethereal solution of XII with diazomethane.

On hydrogenation of 3.0 g. of the methyl ester of XII over palladium-on-charcoal in absolute alcohol at 2–3 atmospheres of hydrogen pressure a marked drop in rate of absorption occurred after one equivalent had been absorbed. After removal of the catalyst and concentration there was obtained 1.85 g. (70%) of the lactone of  $\beta$ -(1-hydroxy-2,2,6-trimethylcyclohexyl)acrylic acid, m.p. 104.8–106.0°. Recrystallization afforded a pure sample, m.p. 107.8–108.2°.

*Anal.* Calc'd for  $C_{12}H_{18}O_2$ : C, 74.2; H, 9.3.

Found: C, 74.2; H, 9.2.

*Lactone of  $\beta$ -(1-hydroxy-2,2,6-trimethylcyclohexyl)propionic acid.* To a suspension of 5.25 g. (0.025 mole) of XII in 250 cc. of liquid ammonia was added 1.16 g. (0.05 mole) of sodium in small bits. At this point the solution was not blue. Further addition of 0.06 g. of sodium produced a blue color which faded after about 30 minutes. Enough additional sodium was added so that a total of 4.6 g. (0.2 mole) was present. After stirring for four hours (still blue) 11.8 g. of powdered ammonium chloride was added and the ammonia was allowed to evaporate. Soxhlet extraction of the residue with ether yielded a material which, when

treated with a solution of sodium bicarbonate, left 1.45 g. of insoluble residue. By crystallization of this and other fractions of the reaction mixture there was obtained an appreciable amount of a neutral material, m.p. 80-81°, which consumed alkali in alcohol. A Zerewitinow test showed no active hydrogen. Analysis indicated the formula  $C_{12}H_{20}O_2$  and we believe that this compound has the structure of the lactone as indicated. We did not repeat this experiment.

Anal. Calc'd for  $C_{12}H_{20}O_2$ : C, 73.4; H, 10.3.

Found: C, 73.6, 73.7; H, 10.4, 10.3.

TABLE I  
CATALYTIC HYDROGENATION OF SOME ACETYLENIC COMPOUNDS

COMPOUND	TYPE OF HYDROGENATION WITH	
	Pt <sup>a</sup>	Pd <sup>b</sup>
I. $HOCH_2C\equiv CC(OH)(CH_3)CH_2CH_2OCH_3$ .....	NS <sup>c</sup>	SH <sup>d</sup>
VI. $CH_3COOCH_2C\equiv CC(OH)(CH_3)CH_2CH_2OCH_3$ .....	H <sup>e</sup>	H
VII. $HOCH_2C\equiv CC(CH_3)=CHCH_2OCH_3$ .....	NS	S'
VIII. $CH_3COOCH_2C\equiv CC(CH_3)=CHCH_2OCH_3$ .....	H	H
IX. $R(OH)C\equiv CCOCH_3^g$ .....	NR <sup>h</sup>	NR
X. $R(OH)C\equiv CH$ .....	NS	SH
XI. $R'C\equiv CCOCH_3^i$ .....	NS	S'
XII. $R''(OH)C\equiv CCOOH^k$ .....	D <sup>l</sup>	D
XIII. $R''(OH)C\equiv CCOOC_2H_5(CH_3)$ .....	SH	SH
XIV. $C_3H_7C\equiv CCOOH$ .....	NS	SH
$HC\equiv CCH_2OH$ .....	NS	SH
$HC\equiv CCH_2CH_2OH$ (19).....	NS	NS
$HC\equiv CCH_2OCOCH_3$ .....	H	H
$HC\equiv CCH_2CH_2OCOCH_3$ .....	NS	NS
$(CH_3)_2C(OH)C\equiv CC(OH)(CH_3)_2$ .....	SH	SH

<sup>a</sup> Adam's platinum oxide. <sup>b</sup> Palladium-on-charcoal, prepared according to (1) or, in some cases using I, Linstead and Thomas, *J. Chem. Soc.*, 1127 (1940). <sup>c</sup> NS, nonselective hydrogenation to saturated analog. <sup>d</sup> SH, selective hydrogenation to olefinic analog. <sup>e</sup> H, hydrogenolysis to form acetic acid. <sup>f</sup> S, selective hydrogenation but not as clean cut as in SH. <sup>g</sup> R represents cyclohexylidene radical. <sup>h</sup> NR, no reduction. <sup>i</sup> R' represents the 1-cyclohexenyl radical. <sup>j</sup> The reduction was more selective when a 5% palladium-on-calcium carbonate was used (W. T. Booth, Ph.D. Thesis, OSU, 1947). <sup>k</sup> R'' represents the 2,2,6-trimethylcyclohexylidene radical. <sup>l</sup> D, decarboxylation accompanying reduction. The product formed was not identified, see experimental.

*Preferential hydrogenation studies.* These reductions were carried out in an all-glass semi-micro hydrogenation apparatus similar to that described by Joshel (18). Stirring was accomplished with a magnetic stirrer. The reduction of about 0.2 g. of compound could be followed with ease. It was found expedient to reduce 0.02 g. of catalyst in 50 cc. of ethanol, at which point the sample to be reduced was introduced in a small volume of alcohol through a funneled stopcock. The absorption of hydrogen was carefully followed by noting the rise of the mercury in a graduated burette. All hydrogenations were at room temperature (20-25°) using about a 15-cm. head of mercury for pressure. From the data, rate curves were plotted and used to interpret the selectivity or non-selectivity of the reaction.<sup>6</sup> In most

<sup>6</sup> It is frequently the case that, even though there is no change in rate after one equivalent of hydrogen has been absorbed, the reduction may be quite selective. However, we did not examine the products obtained from experiments designated NS in Table I.



cases at least duplicate runs were made. In some cases similar reductions were carried out on a larger scale to enable careful characterization of products. The results are summarized in Table I.

## SUMMARY

The synthesis of a number of polyfunctional acetylenic compounds is described. The behavior of these compounds on hydrogenation over platinum and supported palladium catalysts is described.

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