Oxidative Coupling of Acetylenic Alcohols

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The oxidative coupling of compounds containing acetylenic hydrogen represents a very useful laboratory method to form a carbon to carbon bond and double the size of the molecule. Acetylenic alcohols have been oxidized with oxygen or air to form the corresponding diacetylenic glycol in aqueous cuprous chloride–ammonium chloride solution[1] and in aqueous amine–amine hydrochloride media.[2]

Although it has been established that cuprous chloride functions as a catalyst for the oxidative coupling, at least 0.25 mole of cuprous chloride per mole of 3-butyn-2-ol was required to obtain the diacetylenic glycol in good (70%) yield after a reaction period of fourteen hours. Similar large requirements for cuprous chloride in the oxidative coupling of propargyl alcohol have also been reported.[2]

Improvements in this technique were desired because (1) large amounts of aqueous cuprous chloride–ammonium chloride solution were employed and (2) some water-insoluble acetylenic alcohols were slow to oxidize. Therefore, a brief study has been made of the use of truly catalytic quantities of cuprous chloride in a pyridine-methanol medium. When 2-methyl-3-butyn-2-ol in pyridine-methanol was oxidized for four hours with air and using 0.025 mole of cuprous chloride per mole of acetylenic alcohol, 2,7-dimethyl-3,5-octadiyne-2,7-diol was formed in 87% yield. Under similar conditions except that only 0.012 mole of cuprous chloride was employed per mole of acetylenic alcohol and air was replaced by oxygen, the diol was isolated in 90% yield after a reaction period of only two and one-half hours. Propargyl alcohol (1 mole) was oxidized with oxygen using only 0.016 mole of cuprous chloride to form 2,4-hexadiyne-1,6-diol in 75% yield. Under similar conditions, 4-hexen-1-yn-3-ol was coupled to produce 2,10-dodecadiene-5,7-diyne-4,9-diol in 66% yield. These results show that a primary secondary and tertiary acetylenic alcohol can each be oxidatively coupled in good yield using truly catalytic amounts of cuprous chloride.

The oxidation of 1-methoxy-1-butene-3-yne to form 1,8-dimethoxy-1,7-octadiene-3,5-diyne has been accomplished with small amounts of cuprous chloride in the presence of pyridine.[3] Acetylenic hydrocarbons have also been coupled under similar conditions.[4,5]

EXPERIMENTAL

The following procedure illustrates the method employed to obtain the results summarized above.

A mixture of 2-methyl-3-butyn-2-ol (84 g., 1.00 mole), pyridine (20 g., .25 mole), methanol (78 g.) and cuprous chloride (1.2 g., .012 mole) was stirred at 30–35° for 2.5 hr. while oxygen was passed through the liquid at the rate of 10 l./hr. The oxygen absorption had ceased by this time and a total of 7 l. (0.28 mole) of oxygen had been absorbed. The mixture was poured into 400 ml. of saturated ammonium chloride solution and extracted with ethyl ether. The extract was washed with sodium carbonate solution, dried with magnesium sulfate and evaporated to dryness on the steam bath. The crude diol (77g.) was crystallized from 1200 ml. of benzene to obtain 75 g. (90% yield) of 2,7-dimethyl-3,5-octadiyne-2,7-diol of m.p. 127–129°.

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Attempted Preparation of 2-Azabicyclooctatriene[1]

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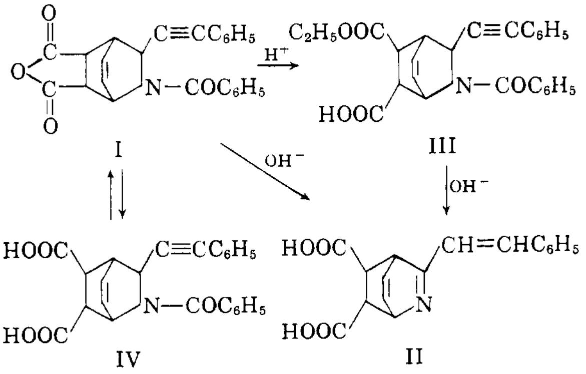
Recent interest in barrelene, bicyclo[2.2.2]octatriene, prompted us to seek analogs containing nitrogen.[4] In several exploratory experiments we failed to dehydrogenate 1,4-diazabicyclo[2.2.2]-octane. More extensive work with 2-azabicyclo compounds[5] indicated that if an octatriene (VII) was obtained, it fell apart under the conditions of the experiments.



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(3) Support from a Research Participation Program of the National Science Foundation is gratefully acknowledged.

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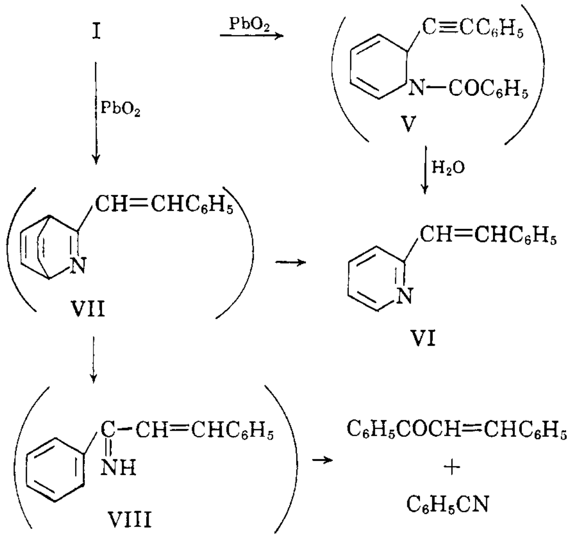
The preparations of *N*-benzoyl-3-phenylethynyl-7,8-dicarboxyanhydride-2-azabicyclo[2.2.2]5-octene (I) and one hydrolysis product have been described.[5] Now three additional hydrolysis products are reported.

Three approaches to the 2-azabicyclo[2.2.2]-octatriene system were examined. Electrolysis[6] of II led to undefined products. The reaction of I with lead tetraacetate in decalin gave II; the reaction of II with lead tetraacetate in benzene-pyridine gave benzaldehyde and benzoic acid.[7] Treatment of I with lead dioxide led to benzaldehyde, benzoic acid, stilbazole (VI), benzonitrile, and benzalacetophenone.[8] The following scheme in which V, VII, and VIII are possible intermediates is proposed to account for the lead dioxide products.



The formation of the styryl residue in VII parallels the hydrolyses I → II and V to VI which have been described previously.[5] Two modes of ring cleavage of VII appear to be necessary to account for the products. In fact, the proposed intermediate VIII appears to be a highly plausible precursor of benzalacetophenone and benzonitrile.

Unfortunately the timing of the decarboxylations step cannot be established from our work. This makes reaction paths through the 2-azabicyclooctatriene uncertain. Thus, VII is plausible but speculative. What is clear, however, is that if VII did form, it did not survive.

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses are by Micro Tech Laboratories, Skokie, Ill.

N-Benzoyl-3-phenylethynyl-7,8-dicarboxyanhydride-2-azabicyclo[2.2.2]-5-octene (I). As described previously, V was prepared from silver phenylacetylide, benzoyl chloride, and pyridine in carbon tetrachloride.[5] The yields of V were erratic unless the crude product was first taken up in benzene and thoroughly washed with dilute acid, ammonium hydroxide, and water. After the benzene solution was evaporated to dryness, the residue was taken up in hot Skelly B from which a 78% yield of V could be obtained. I was obtained by refluxing a benzene solution containing either crude or purified V with maleic anhydride overnight. Alternatively I was obtained by melting V and maleic anhydride together with stirring at *ca.* 100–150°. The m.p. of I was 217–219° (lit.[5] 217–219°).

N-Benzoyl-3-phenylethynyl-7,8-dicarboxy-2-azabicyclo[2.2.2]5-octene (IV). This was a minor coproduct in the synthesis of I which was sparingly soluble in acetone and chloroform. It was found in the basic extracts and recrystallized from methanol as white crystals m.p. 196–205°.

Anal. Calcd. for $C_{24}H_{19}O_5N$: C, 71.80; H, 4.77; Found: C, 71.17; H, 4.70. Heating IV at 220° for 5–10 min. gave a quantitative yield of I.

3-Styryl-7,8-dicarboxy-2-azabicyclo[2.2.2]2,5-octadiene (II). I (15 g.) was treated with sodium hydroxide in aqueous ethanol for 2 hr. on the steam bath; 9.7 g. of II, m.p. 233–240, was obtained. The analytical sample, crystallized from chloroform, was white and had m.p. 239–240°.

Anal. Calcd. for $C_{17}H_{15}O_4N$: C, 68.68; H, 5.09. Found: C, 68.96; H, 5.22.

In the previous paper[5] it was reported that basic hydrolysis gave a compound with the same elemental analysis as II but with m.p. 195–196°. It is probable that these are two of the four possible geometric isomers of II.

N-benzoyl-3-phenylethynyl-7,8-dicarboxy-2-azabicyclo-[2.2.2]5-octene-monoethyl ester (III). I (3.7 g.) was treated with hydrochloric acid in ethanol for 1.5 hr. at reflux. Two grams of crude III were obtained. The analytical sample, crystallized from chloroform was white and had m.p. 176–179°.

Anal. Calcd. for $C_{26}H_{23}O_6N$: C, 72.71; H, 5.40. Found: C, 72.80; H, 5.41. It is not clear whether the 5- or 6- position has the carbethoxy group. Further treatment of the tail fractions with base gave II in almost theoretical yield. Similarly, basic hydrolysis of III gave II.

Attempted Dehydrogenation to 1,4-diazabicyclooctatriene The starting material, 1,4-diazabicyclo[2.2.2]octane or Dabco, was a gift of the Houdry Process Corp. Attempts to dehydrogenate Dabco with sulfur, nitrobenzene, mercuric oxide, chloranil in various solvents or over palladium(5%)-asbestos in a nitrogen stream containing benzene or benzene and ethylene failed.

Electrolysis of II. A methanolic solution of II (2.5 g.) and sodium methoxide (0.5 g.) was electrolyzed at *ca.* 2.0 amp. and 30–35 volt for 2 hr. between platinum electrodes. Apart from small amounts of starting material, the product mixture could not be resolved.

Oxidations of I *and* II.[7,8] (a) Treatment of I (1.9 g.) with lead tetraacetate (5 g.) with benzene (60 ml.), pyridine (10 ml.), and water (0.2 ml.) for 2 hr. at reflux led chiefly to I and II. (b) Treatment of II (11 g.) with lead tetraacetate (20 g.) in benzene-pyridine (4:1) at 60–70° for 3 hr. under nitrogen gave some starting material and benzoic acid and a complex liquid mixture. (c) I (45 g.), lead dioxide (70 g. Baker's Analyzed grade), and sand (75 g.) were heated gradually in a stream of nitrogen; carbon dioxide evolution set in about 196°. The temperature was held at 250° for *ca.* 0.5 hr. The volatile components (20–25 ml.) condensed in a trap. This oil was fractionated and the fractions individually examined. Gas chromatography and infrared analysis as well as picric acid and 2,4-dinitrophenylhydrazone tests were used. The presence of ethanol, benzaldehyde, benzoic acid, benzonitrile, and possibly pyridine was established. The picrate of stilbazole, m.p. 213–215°, was obtained: it did not depress the m.p. of an authentic sample. The DNP of benzalacetophenone m.p. 245° was isolated and showed no depression with an authentic sample (d) Treatment of I in decalin gave some II.

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