The Formic Acid Rearrangement of 2-Cyclohexyl-3-butyn-2-ol

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The present work, as well as the several reports from this laboratory[1,3], was directed to exploring the effect of the structure of tertiary ethynylcarbinols on the course of Rupe reaction.

Here, 2-cyclohexyl-3-butyn-2-ol (II) was chosen for another model carbinol in which R_1 (or R_2; R_1, R_2=alkyl; I) is secondary and, at the same time, R_2 (or R_1) is not primary.

$$R_1-\underset{\displaystyle OH}{\overset{\displaystyle R_2}{C}}-C\equiv CH$$

(I)

It was previously shown[1] that the tertiary ethynylcarbinols may be classified into two groups in relation to Rupe reaction. One group involves the carbinols in which R_1 or R_2 is primary or secondary. They are capable of undergoing dehydration followed by hydration (at the ethynyl group), and afford chiefly ketones as the reaction product; the formation of aldehydes is generally of a small quantity.

The other group consists of the carbinols in which both R_1 and R_2 are neither primary nor secondary. They undergo mainly Meyer-Schuster rearrangement to yield aldehydes. Seemingly, the methyl group which is adjacent to the carbon atom attached to the hydroxyl group plays a role somewhat similar to the tertiary alkyl viewed from the several instances already reported[2]; the dehydration between the methyl group and the neighboring hydroxyl group seems to occur actually, however the formation of ketones is inconsiderable.

Though the carbinols such as II belong to the first group, they have only one hydrogen atom on the concerned carbon atom (adjacent to the carbon atom attached to the hydroxyl group). The question whether such a carbinol has, to a certain degree, a tendency suitable for yielding aldehydes besides ketones is now under investigation. Of course, such a trend may not necessarily result only from the above structure, however it was observed on the two model carbinols of this type. One is 3, 4-dimethyl-1-hexyn-3-ol, from the reaction products of which 3, 4-dimethyl-2-hexenal was easily isolated by simple distillation[3] (ca. 3% yield, a small but significant quantity). The other is II in the present experiment, which gave 3-cyclohexyl-2-butenal(IV) in ca. 12% yield in addition to 3-cyclohexylidene-2-butanone(III) (ca. 28% yield). That such a considerable amount of the aldehyde could easily be isolated, may be noteworthy compared with other carbinols which are capable of undergoing the usual Rupe reaction. There are of course some reports[4] regarding the isolation of aldehydes (up to ca. 10%) from the reaction products

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[1] T. Takeshima, *J. Sci. Research Inst.*, **45**, 211 (1951); ibid., **47**, 237 (1953); ibid., **48**, 103, 113 (1954); *J. Am. Chem. Soc.*, **75**, 4107 (1953).

[2] C. D. Hurd and W. D. McPhee, ibid., **71**, 398 (1949); T. Takeshima, *J. Sci. Research Inst.*, **48**, 113 (1954).

[3] T. Takeshima, *J. Am. Chem. Soc.*, **75**, 3309 (1953).

[4] F. G. Fischer and K. Löwenberg, *Ann.*, **475**, 183 (1929); J. D. Chanley, *J. Am. Chem. Soc.*, **70**, 244 (1948).

TABLE I

REACTION PRODUCTS FROM II

Fraction	B. p., °C (30 mm.)	Yield, g., from 20 g. of II	Constituent
1	75~80	ca. 2.5	Cyclohexanone and possibly 3-cyclohexylidene-1-butyne
2	81~95 (81~85)*	ca. 3.2	III and possibly 3-cyclohexylidene-1-butyne
3	ca. 100~130 (ca. 105~110)*	ca. 5.5	III predominating
4	132~138 (ca. 135)*	ca. 2.3	IV

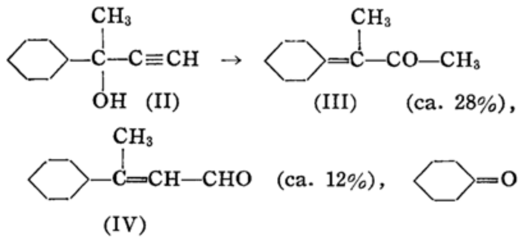
* The boiling point enclosed with parentheses shows the one at which the greater part of the fraction distilled out.

DERIVATIVES OF THE CARBONYL COMPOUNDS

Original compd.	2, 4-Dinitrophenylhydrazone		Semicarbazone	
	M. p., °C	Appearance	M. p., °C	Appearance
III	123~124	Deep yellow crystals	174~175	Colorless needles
IV	199~200	Light red long plates	183~184 (slow heating) ca. 196 (rapid heating)	Colorless long plates
V	125~127	Deep yellow crystals	139~140	Colorless plates

	Dimedone Derivative	
	M. p., °C	Appearance
IV	160~161	Colorless crystals

of the carbinols which have secondary carbon atom in the concerned position.



The present experiment is outlined as follows. II was refluxed with ca. 80% formic acid and treated in the usual manner. The reaction products were distilled and four fractions were collected (consult Table I). The low-boiling fraction (fraction 1) contained a considerable amount of cyclohexanone, which, considering the fact mentioned below, seemed to owe its origin to the acid hydrolysis of III. The greater part of fraction 3 consisted of a carbonyl compound III which gave the ketonic derivatives shown in Table I. III, one of the two main products in this reaction, was practically indifferent toward Schiff reagent, had unsaturated nature, and gave pyrazoline derivative. Further, III on hydrolysis by acid gave cyclohexanone and methyl ethyl ketone as their 2, 4-dinitrophenylhydrazone. Thus III proved to be 3-cyclohexylidene-2-butanone. Though the boiling point of III corresponded to the one reported by Thakur[5)], the melting point of its semicarbazone was quite different from the one obtained by him.

Fraction 4, which had a pleasant smell, proved to consist of a carbonyl compound IV of formula $C_{10}H_{16}O$ of which derivatives are shown in Table I. The compound had an unsaturated aldehydic nature. On treatment with phenylhydrazine, it readily gave an oily product which had a pyrazoline reaction of a coloration different from that of III. Further, ozonolysis gave glyoxal as the 2, 4-dinitrophenylosazone. Hydrogenation afforded the corresponding saturated compound V which had an intensely positive test with Schiff reagent. Thus structure IV, 3-cyclohexyl-2-butenal, and V, 3-cyclohexylbutyraldehyde, were assigned to these two compounds, respectively.

Finally, fraction 1 seemed to contain, besides cyclohexanone, a non-ketonic substance of unsaturated nature. Likewise, fraction 2, in which some quantity of cyclohexanone and III was detected as

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5) R. S. Thakur, *J. Chem. Soc.*, **1933**, 1481. He obtained the ketone by a different route, and reported three melting points of somewhat indefinite nature for its semicarbazone, one distinct melting point being obtained after fractional recrystallization. The one in the present experiment was believed to be of the single compound.

their 2,4-dinitrophenylhydrazones, also contained the same substance. It was inferred from the behavior of these two fractions (see experimental part) that the compound is possibly 3-cyclohexylidene-1-butyne.

Experimental

2-Cyclohexyl-3-butyn-2-ol. — The carbinol was prepared by ethynation of acetylcyclohexane in the usual manner[1] using sodium amide as the reagent. Yield ca. 83%, b. p. 104∼106° (18 mm.) (reported b. p. 106∼110° (23 mm.)[6]); practically no ketonic compound was detected in this fraction by the 2,4-dinitrophenylhydrazine test. Fairly good yield could be thus obtained without depending on the liquid ammonia method[6]; in the present preparation acetylene was passed through for ca. 12 hr. at ca. −7° and the reaction mixture was then left overnight in an ice-box.

The original **acetylcyclohexane** was prepared by hydrogenating 1-acetylcyclohexene with palladium; b. p. 178∼180°, yield 86%.

1-Acetylcyclohexene was prepared from 1-ethynylcyclohexanol with the aid of its acid rearrangement[7]; 130 g. of the carbinol was treated with a mixture of 12 g. of sulfuric acid, 280 g. of acetic acid and 2 g. of water. On heating, a vigorous spontaneous reaction was initiated; a large reflux condenser was preferably fitted; the heating must be stopped immediately after the initiation and the reaction, if needed, was moderated by cooling with water. The pure ketone could be obtained by this method, which contained practically no aldehyde; b. p. 110∼111° (50 mm.), yield 65%.

The Formic Acid Rearrangement of 2-Cyclohexyl-3-butyn-2-ol (II). — Twenty grams of II was gently refluxed with 160 g. of ca. 80% formic acid for ca. 1 hr.; the heating was interrupted during the spontaneous boiling at the beginning. The reaction mixture was left to be cooled, and then neutralized with a concentrated solution of potassium carbonate, extracted with ether, dried by potassium carbonate, the ether driven off, and distilled collecting the following fractions. (1) b. p. 75∼80° (30 mm.), ca. 2.5 g.; (2) b. p. 81∼95° (30 mm.), ca. 3.2 g. (the greater part distilled out at 81∼85° (30 mm.)); (3) b. p. ca. 100∼130° (30 mm.), ca. 5.5 g. (ca. 28%; the greater part distilled out at ca. 105∼110° (30mm.)); (4) b. p. 132∼138° (30 mm.), ca. 2.3 g. (ca. 12%; the greater part distilled out at ca. 135° (30mm.)); Distillation residue, tarry material

All these fractions were colorless, scarcely soluble in water, easily soluble in common organic solvents, and had a smaller density than water at room temperature.

Fraction 1 gave considerable quantity of cyclohexanone 2,4-dinitrophenylhydrazone, which on recrystallization from hot ethanol melted at 158∼160° and did not depress the melting point of an authentic sample (Found: C, 51.72; H, 5.08; N, 19.81%). Another 2,4-dinitrophenylhydrazone obtained from this fraction, perhaps that of III, was only of a small quantity; it was difficult to obtain any derivative from the same fraction by treating it, as it is, with semicarbazide reagent. It, as it is or as the ethanolic solution, readily decolorized bromine water; II apparently had much more inertia toward this reaction, and had a much higher boiling point than this fraction. Further, it gave some precipitates with ammoniacal silver nitrate (fraction 3 and 4 gave practically no precipitates), gave red halochromism with sulfuric acid, and turned yellowish on a few hour's standing and also turned viscous on long standing. Analyses and molecular weight measurement of this fraction gave intermediate values between cyclohexanone and 3-cyclohexylidene-1-butyne.

Anal. Found: C, 81.07; H, 9.95; mol. wt., (Rast), 130. Calcd. for $C_6H_{10}O$ (cyclohexanone): C, 73.43; H, 10.27; mol. wt., 98.1. Calcd. for $C_{10}H_{14}$ (3-cyclohexylidene-1-butyne); C, 89.49; H, 10.51; mol. wt., 134.2. Calcd. for $C_{10}H_{16}O$ (III): C, 78.90; H, 10.60%; mol. wt., 152.2.

Fraction 2 had properties similar to those of fraction 1; the quantity obtained of cyclohexanone 2,4-dinitrophenylhydrazone was less than that from the latter, and, in addition, some amount of 2,4-dinitrophenylhydrazone of III was obtained.

Fraction 3 (III).—The fraction was redistilled, collecting ca. 3 g. of a fraction boiling at 105∼110° (30 mm.). Most part of it consisted of 3-cyclohexylidene-2-butanone (III), which was ascertained from the quantity obtained of the 2,4-dinitrophenylhydrazone. It was only weakly positive toward Schiff reagent, readily decolorized bromine water, gave practically no precipitates with ammoniacal silver nitrate, and did not reduce Fehling solution. It gave a positive test for methyl ketone[8], fuchsine-red color being produced on heating with potassium hypobromite solution and pyridine. On refluxing the same fraction for ca. 1.5 hr. with a solution of phenylhydrazine hydrochloride in ethanolic acetic acid, colorless crystals were produced, which gave a pyrazoline reaction of wine-red coloration with sulfuric acid and sodium nitrite; the crystals were very easily soluble in aqueous methanol.

2,4-Dinitrophenylhydrazone of III was recrystallized from methanolic pyridine, deep yellow needles or crystals, easily soluble in pyridine, m. p. 123∼124°.

Anal. Found: C, 57.53; H, 5.82; N, 16.83. Calcd. for $C_{16}H_{20}O_4N_4$: C, 57.82; H, 6.07; N, 16.86%.

Semicarbazone of III was recrystallized from methanol, colorless needles somewhat soluble in the same solvent, m. p. 174∼175° (indefinite melting points reported[5] are: 180∼184°, 155∼160°, 160∼163° in different preparations; the least soluble semicarbazone in the case of the fractional crystallization, m. p. 192∼193° rapid heating), 187° (slow heating)).

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[6] Domenick Papa, Frank J. Villanits and Helen F. Ginsberg, *Arch. Biochem. Biophys.*, **33**, 482 (1951).

[7] T. Takeshima, *J. Sci. Research Inst.*, **48**, 103 (1954).

[8] J. Adachi, *Anal. Chem.*, **23**, 1491 (1951).

Anal. Found: N, 19.93. Calcd. for $C_{11}H_{19}ON_3$: N, 20.08%.

On adding 2,4-dinitrophenylhydrazine reagent directly to the semicarbazone, the corresponding 2,4-dinitrophenylhydrazone was obtained, which was identical with that of III mentioned above.

Hydrolysis of Fraction 3 (III).—A mixture of 0.5 g. of the above redistilled portion of fraction 3 and 3 cc. of ca. 80% formic acid and 0.5 cc. of 50% sulfuric acid, was boiled under reflux for ca. 3 hr. The reaction mixture was neutralized with a solution of potassium carbonate, extracted with ether, dried with potassium carbonate and distilled. A distillate up to ca. 40°, which consisted almost entirely of the solvent, was rejected. Next ethereal distillate, on treatment with 2,4-dinitrophenylhydrazine reagent, yielded yellow needles which melted at ca. 115°; the melting point was not depressed on admixture with an authentic sample of methyl ethyl ketone 2,4-dinitrophenylhydrazone. The higher boiling distillate, which amounted to a considerable quantity, was converted to cyclohexanone 2,4-dinitrophenylhydrazone which melted at 158~159°; the melting point was not depressed on admixture with the authentic sample.

Fraction 4, b. p. 132~138° (30 mm.), consisted almost only of 3-cyclohexyl-2-butenal (IV), which was ascertained from the quantity obtained of the 2,4-dinitrophenylhydrazone mentioned below. The fraction had a pleasant smell, gave positive test with Schiff reagent (violet color was gradually produced, which was accompanied with a formation of some dregs), reduced ammoniacal silver nitrate, decolorized bromine water, and gave a halochromic coloration with sulfuric acid; a trace of the aldehyde on contact with sulfuric acid turned into deep red and the whole became golden yellow when it was made uniform by shaking; the behavior was somewhat similar to that of III. It, on heating, merely turned Fehling solution into turbid bluish green and the oil became reddish, which seemed to be caused by fine particles of perhaps copper or cuprous oxide; the behavior resembled those of β-methylcrotonaldehyde and 3,4-dimethyl-2-hexenal[9].

It was slightly positive toward methyl ketone test[8], which may be due to contamination with III.

On heating with phenylhydrazine hydrochloride in ethanolic acetic acid, it gave an oily product which had a pyrazoline reaction of dark violet or bluish violet color quite different from that in the case of III.

2,4-Dinitrophenylhydrazone of IV. — The derivative of fraction 4 was recrystallized from pyridine. light red needles or long plates, m. p. 199~200°, easily soluble in hot pyridine and sparingly soluble in cold ethanol.

Anal. Found: C, 57.84; H, 5.91; N, 16.83. Calcd. for $C_{16}H_{20}O_4N_4$: C, 57.82; H, 6.07; N, 16.86%.

Semicarbazone of IV. — The semicarbazone of fraction 4 was recrystallized from methanol, colorless long plates or needles, m. p. 183~184° (slow heating), ca. 196° (rapid heating), easily soluble in hot ethanol.

Anal. Found: N, 20.05. Calcd. for $C_{11}H_{19}ON_3$: N, 20.08%.

The above 2,4-dinitrophenylhydrazone of IV was obtained also from this semicarbazone.

Dimedone Derivative of IV.—To a solution of ca. 0.1 g. of fraction 4 in ca. 4 cc. of 50% ethanol was added ca. 0.6 g. of dimedone and one drop of piperidine, and the mixture then was gently boiled for a while. After being cooled, a small quantity of water was added to the reaction mixture, and the resulting precipitates were collected, recrystallized from aqueous ethanol and then from methanol. Colorless crystals, m. p. 160~161°, fairly soluble in 50% ethanol.

Anal. Found: C, 75.11; H, 9.15. Calcd. for $C_{26}H_{38}O_4$: C, 75.32; H, 9.24%.

Ozonolysis of Fraction 4 (IV).—A solution of 0.5 g. of the fraction in ca. 16 g. of carbon tetrachloride was cooled with ice and ozonized oxygen was passed through for ca. 2 hr., and then the solvent was removed on a water-bath. The viscous product was shaken with aqueous methanol and the oily portion was treated with 2,4-dinitrophenylhydrazine reagent. The dark reddish brown viscous oil produced was recrystallized from methanolic pyridine to yield orange yellow fine needles, m. p. ca. 310°. Reported melting points of glyoxal 2,4-dinitrophenylosazone are: 311~312°[10], 326~328°[11], 318°[12].

Hydrogenation of Fraction 4 (IV). — The fraction was hydrogenated using palladium-kieselguhr catalyst. The greater part of the product distilled out at 112~115° (30 mm.), a colorless liquid which had a camphoraceous odor and produced deep pink color with Schiff reagent. It was considered to be 3-cyclohexylbutyraldehyde (V) and gave the derivatives mentioned below.

2,4-Dinitrophenylhydrazone of V. — It was recrystallized from methanolic pyridine to give deep yellow (tinged with orange) crystals, m. p. 125~127°; mixed melting point with 2,4-dinitrophenylhydrazone of III was 95~103°.

Anal. Found: C, 57.36; H, 6.46; N, 16.66. Calcd. for $C_{16}H_{22}O_4N_4$: C, 57.47; H, 6.63; N, 16.76%.

Semicarbazone of V. — It was recrystallized from methanol, colorless plates, m. p. 139~140°.

Anal. Found: C, 62.40; H, 9.69; N, 20.09. Calcd. for $C_{11}H_{21}ON_3$: C, 62.52; H, 10.02; N, 19.89%.

2,4-Dinitrophenylhydrazone of V was obtained also from the above semicarbazone.

Summary

The formic acid rearrangement of ethynylcarbinols has been extended to 2-cyclo-

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[9] T. Takeshima, *J. Sci. Research Inst.*, **45**, 103 (1951); *J. Am. Chem. Soc.*, **75**, 3309 (1953).

[10] T. L. Jacobs and W. J. Whitcher, ibid., **64**, 2635 (1942).

[11] H. H. Strain, ibid., **57**, 758 (1935).

[12] C. Neuberg and E. Simon, *Biochem. Z.*, **256**, 488 (1932); J. Meisenheimer and W. Schmidt, *Ann.*, **475**, 181 (1929).

hexyl-3-butyn-2-ol(II), a model carbinol in which the tertiary carbon atom and the methyl group are adjacent to the carbon atom attached to the hydroxyl group. The major rearrangement product consisted of a mixture of 3-cyclohexylidene-2-butanone (III) (ca. 28% yield) and a new aldehyde, 3-cyclohexyl-2-butenal(IV) (ca. 12% yield). The latter was hydrogenated to give 3-cyclohexylbutyraldehyde (V). These compounds were isolated and characterized.

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