[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY, COLUMBUS 10, OHIO]

Rearrangement of *trans*- and *cis*-4-*t*-Butyl-1-ethynylcyclohexanols in Formic Acid[1]

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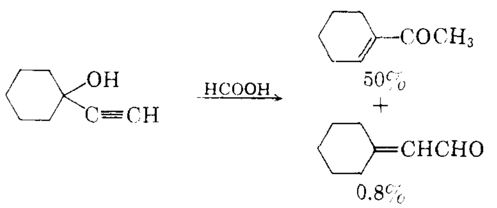
Both *trans* and *cis*-4-*t*-butyl-1-ethynylhexanols (I and II) rearrange to 1-acetyl-4-*t*-butylcyclohexene (III) in high yield on heating with 90% formic acid without forming a trace of isomeric unsaturated aldehyde. Rough kinetic measurements show that II (hydroxyl group axial) is converted into III more rapidly than is I. 4-*t*-Butyl-1-ethynylcyclohexene (IV) is converted into III more rapidly than either I or II and hence is a likely intermediate in the rearrangements of I and II. The simultaneous conversion of I and II to their formate esters under the reaction conditions used complicates the kinetic picture. 1-Acetyl-4-*t*-butylcyclohexene (III) and 1-acetylcyclohexene fail to give positive iodoform tests.

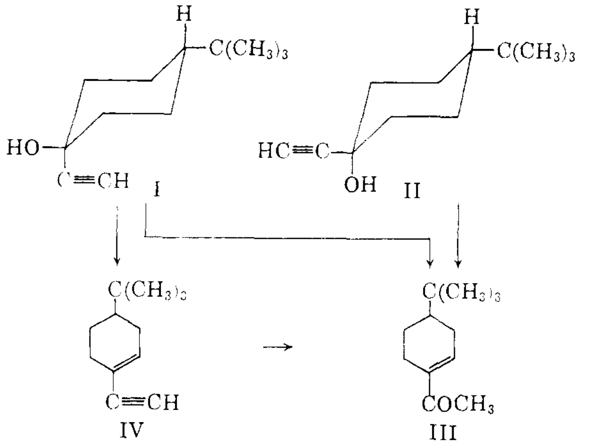
The rearrangement of 1-ethynylcyclohexanol on treatment with formic acid is known to yield mainly 1-acetylcyclohexene together with a small amount of cyclohexylideneacetaldehyde.[2] We thought it possible that the ketone arose from one conformation and the aldehyde from the other.



To test this hypothesis, the two isomeric 4-*t*-butyl-1-ethynylcyclohexanols[3] (I) (*trans* with regard to hydroxyl and *t*-butyl groups) and (II) (*cis*) were prepared and rearranged under identical conditions. These compounds were chosen since the undoubtly equatorial *t*-butyl group ensures that the hydroxyl group is equatorial in I and is axial in II.[4]

On treatment of I and II with formic acid at reflux the main product in each case was 1-acetyl-4-*t*-butylcyclohexene (III). No trace of aldehyde, as judged by a negative Tollens test and n.m.r. analysis,[5] was obtained with the entire reaction products in either case. The structure of III was supported by infrared, ultraviolet and nuclear magnetic resonance[6] spectral determinations. Thus our hypothesis that the conformation of the starting alcohols was of importance in determining the structure of the product was shown to be false.

In order to test whether 4-*t*-butyl-1-ethynylcyclohexene (IV) might be a common intermediate for the conversion of the isomeric ethynylcyclohexanol I and II into the unsaturated ketone[7] III, some rough kinetic measurements were made on I, II and IV.



I II IV III

cis-4-*t*-Butyl-1-ethynylcyclohexanol (II) was converted into 1-acetyl-4-*t*-butylcyclohexene (III) more rapidly than was I. This fact supports the assignment of structure for I and II previously made,[3] as one would expect more rapid dehydration of the isomer containing the axial hydroxyl group.[8] Furthermore, 4-*t*-butyl-1-ethynylcyclohexene (IV) was converted to 1-acetyl-4-*t*-butylcyclohexene (III) more rapidly than either I or II. Hence IV is a likely intermediate in the conversion of I and II into III.

By stopping the reactions involving the ethynylcyclohexanols I and II before they had gone to completion, it has shown that appreciable amounts of the formic acid esters of I and II were present. Thus the kinetic picture is complicated by the facts that the alcohols I and II may be in part directly converted into eneyne IV and partly esterified to the corresponding formates[9] which then lose formic acid to yield eneyne IV. The work we have done does not prove that all of the 1-acetyl-4-t-butylcyclohexene III is formed *via* IV,[10] but probably most is. This work supports the mechanism previously advanced[7] for the Rupe rearrangement in formic acid solution.

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[1] The work herein described formed part of the M.S. Thesis of P. H. G., 1959.

[2] See J. D. Chanley, THIS JOURNAL, **70**, 244 (1948), for a critical review of earlier work.

[3] G. F. Hennion and F. X. O'Shea, *ibid.*, **80**, 614 (1958).

[4] S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955).

[5] We are indebted to Dr. George Slomp, The Upjohn Co., for the nuclear magnetic resonance analysis of the crude materials.

[6] We thank Dr. G. V. D. Tiers, Minnesota Mining and Manufacturing Co., for this determination and interpretation.

[7] G. F. Hennion, R. B. Davis and D. E. Maloney, THIS JOURNAL, **71**, 2813 (1949), reported qualitative evidence for an eneyne intermediate in the rearrangement of ethylmethylethynylcarbinol.

[8] No previous data on rates of dehydration of axial and equatorial tertiary alcohols was found. However, for secondary alcohols, axial isomers are dehydrated more rapidly than the equatorial; see G. Vavon and M. Barbier, *Bull. soc. chim.*, [4] **49**, 567 (1931), and D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).

[9] In the case of ethylmethylethynylcarbinol, Hennion, *et al.*,[7] showed that the corresponding formate was thermally stable but that the acetate gave rearranged unsaturated ketone on treatment with hot formic acid.

[10] In the rearrangement of 1-ethynylcyclohexanol to 1-acetylcyclohexene catalyzed by a sulfonated styrene resin, 1-ethynylcyclohexene, was shown *not* to be an intermediate; M. S. Newman, THIS JOURNAL, **75**, 4740 (1953).

Experimental[11]

***Trans*- and *cis*-4-*t*-Butyl-1-ethynylcyclohexanols** (I and II).—A mixture[12] of I and II was separated into pure *trans*-4-*t*-butyl-1-ethynylcyclohexanol (I), m.p. 101.3–102.3°, and pure II, m.p. 63.0–64.0°, essentially as described.[3] During the separation, a sample of 4-*t*-butylcyclohexanone[4] was obtained and converted into its 2,4-dinitrophenylhydrazone, m.p. 151.9–153.2°.

Anal. Calcd. for $C_{16}H_{22}N_4O_4$: N, 16.8. Found: N, 16.7.

Rearrangements of I and II into 1-Acetyl-4-*t*-butylcyclohexene (III).—A solution of 1.06 g. of *trans*-alcohol I in 4.6 ml. of 90% formic acid was heated at reflux for 45 minutes, then cooled and poured on ice. By extraction with ether-benzene and washing this extract with alkali, there was isolated 1.03 g. of a pale yellow oil. This oil was estimated to have between 4 and 8% of acetylenic hydrogen by testing as follows. A small amount of pure I was dissolved in 1:1 alcohol–water and a portion was treated with 2.5% silver nitrate solution. The resulting solution was tested with universal type indicator paper, a change in color from orange to orange-red indicating acidity. The original solution was then diluted before testing as above until the color change no longer occurred. Then, a solution of the same amount of unknown (yellow oil) was tested similarly and diluted until the test was no longer positive. This test does not distinguish starting ethynyl alcohol I from 4-1-butyl-1-ethynylcyclohexene (IV), but is fairly sensitive for showing the presence of acetylenic hydrogen.

A portion of the above pale yellow oil yielded the red 2,4-dinitrophenyl-hydrazone of 1-acetyl-4-*t*-butylcyclohexene in 72–78% yield. The pure derivative, purified by chromatography over alumina using benzene, melted at 178.2–179.0°.

Anal. Calcd for $C_{18}H_{24}N_4O_4$: C, 60.0; H, 6.7. Found: C, 60.3; H, 6.7.

When 0.33 g. of *cis*-alcohol II in 1.45 ml. of 90% formic acid was heated at reflux for 45 minutes, a workup similar to that above provided 0.32 g. of pale yellow oil. This oil gave no test for acetylenic hydrogen when tested as described above and the yield of 2,4-dinitrophenylhydrazone indicated about a 95% yield of III. The purified derivative, m.p. 177.0–178.0°, was identical to that prepared above.

An examination by n.m.r. of the entire crude pale yellow oil obtained from another run with *trans*-I indicated that no aldehydic hydrogen was present.[5]

1-Acetyl-4-*t*-butylcyclohexene (III).—A solution of 10 g. of I in 46 ml. of 90% formic acid was held at reflux for 1.5 hours. Dilution with water followed by extraction with ether afforded the crude product in almost quantitative yield. The analytical sample, b.p. 135–137° at 14 mm., was obtained in 75% yield.

Anal. Calcd for $C_{12}H_{20}O$: C, 80.0; H, 11.2. Found: C, 80.2, 80.4; H, 10.7, 10.9.

1-Ethynyl-4-*t*-butylcyclohexene (IV).—To a solution of 5.6 g. of I in 6 ml. of dry pyridine was added a solution of 2.4 ml. of phosphorus oxychloride in 2.4 ml. of pyridine. After warming to 65° for 20 minutes the product was isolated by ether extraction and distilled to yield 0.9 g. (18%) of IV, b.p. 64–67° at 9 mm. Redistillation yielded an analytical sample as a colorless oil, n^{25}_{D} 1.4850.

Anal. Calcd for $C_{12}H_{18}$: C, 88.8; H, 11.2. Found: C, 88.3; H, 11.6.

Rough Kinetic Measurements.—The rates of reaction of I, II and IV with the same batch of approximately 90% formic acid at about 79° (b.p. of carbon tetrachloride) were estimated by following the change in absorption at 234 mμ. Aliquots, suitably diluted with alcohol containing sufficient piperidine to neutralize the formic acid, were taken after 20, 110, 255 and 450 minutes. The percentage of 4-*t*-butyl-1-acetylcyclohexene (III) was estimated by using the molar extinction coefficients obtained from the aliquots and comparing with that obtained after the 450-minute interval after which time no further change occurred. The molar extinction coefficient at 234 mμ of both final solutions was almost the same (10,600). The extinction coefficient of 4-*t*-butyl-1-ethynylcyclohexene (IV) at 234 mμ is 6100 and is maximal (8900) at 223 mμ. No corrections for possible variations from Beer's law were made. These experiments showed that the *cis*-isomer II reacts considerably more rapidly than the *trans* isomer I. For example, after 20 and 110 minutes, compound I had yielded 17 and 71% of III, whereas II had yielded 38 and 90% of III. Under similar conditions after 20 minutes 4-*t*-butyl-1-ethynylcyclohexene (IV) had almost completely reacted to form III.

The infrared absorption spectra of samples of crude product obtained by quenching reaction mixtures of both I and II with 90% formic acid at 50° after 15 minutes showed a band at 5.75μ characteristic of formate esters,[13] in addition to hydroxyl bands.

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[11] All melting points are uncorrected. Analyses by Galbraith Laboratories, Knoxville, Tenn.

[12] We thank the Air Reduction Chemical Co., Murray Hill, N. J., for a supply of the mixed isomers, and Miss C. Gedeist for aid in separation of the isomers.

[13] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., London, 1954, p. 179ff.

[Contribution from the Department of Chemistry, Massachusetts Institute of Technology]

The Reaction of Ketones with Diazomethane

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The reactions of diazomethane with benzil, biacetyl, acetophenone, benzyl methyl ketone, 3,3-dimethyl-2-butanone, 3-methyl-2-butanone, 2-pentanone and 4-methyl-3-penten-2-one have been studied. Use of boron trifluoride as a catalyst for these reactions was found to accelerate markedly the reactions and to favor the formation of ketones rather than other products. The ratios of ketonic products obtained from these reactions suggest the order of migratory aptitudes: $C_6H_5 \sim (CH_3)_2C{=}CH > CH_3 \sim CH_3CH_2CH_2 > (CH_3)_2CH \sim C_6H_5CH_2 \sim (CH_3)_3C$. Similar product ratios were obtained from the semipinacolic deamination of the appropriate 1,1-disubstituted-2-aminoethanols.

The reaction of diazomethane with ketones[3,4] is usually considered to follow the course illustrated in the accompanying equations. The diazonium ion II, also a probable intermediate in the semipinacolic deamination of amino alcohols of the type V,[5-7] is believed to lose nitrogen with the si-

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[1] Eastman Kodak Predoctoral Fellow, 1958–1959.

[2] Monsanto Chemical Co. Predoctoral Fellow, 1958–1959.

[3] C. D. Gutsche, *Org. Reactions*, **8**, 364 (1954).

[4] B. Eistert in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, pp. 513–570.

[5] M. Tiffeneau and H. Cahnmann, *Bull. soc. chim. France*, [5] **2**, 1876 (1935).

[6] D. Y. Curtin and M. C. Crew, This Journal, **76**, 3719 (1954).

[7] H. O. House and E. J. Grubbs, *ibid.*, **81**, 4733 (1959).