

**Investigation of Possible Phenyl Participation in the Oxy-Cope and Acetylenic
Oxy-Cope Rearrangements**

By

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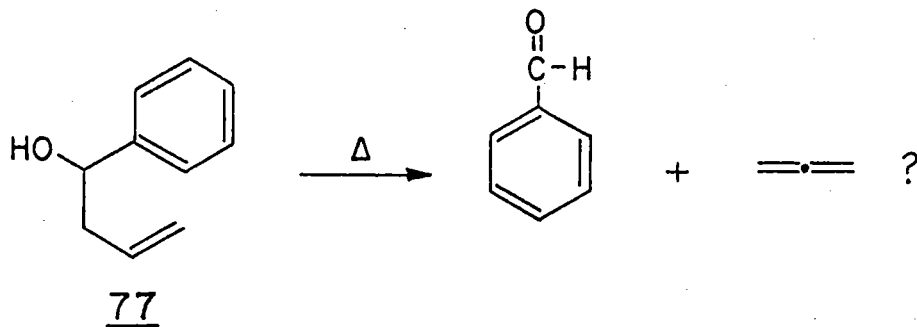
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Abstract:

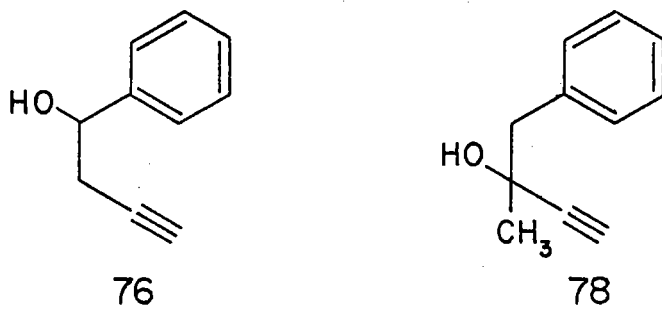
Vapor phase thermolysis of 1-phenyl-3-butyn-1-ol and 1-phenyl-2-methyl-3-butyn-2-ol in the gas phase or liquid phase failed to yield the expected oxy-Cope products, even at elevated temperatures and protracted reaction times. 1-Phenyl-3-butyn-1-ol cleaved to benzaldehyde and allene, while 1-phenyl-2-methyl-3-butyn-2-ol was completely unreactive. The data indicate that the disruption of the aromatic ring necessary for the Oxy-Cope reaction to occur results in too high an activation energy. Claisen Rearrangements, by contrast, proceed readily under these conditions. The activating effect of the ether oxygen atom in Claisen rearrangements may lower their activation energy compared to oxy-Cope systems.

Investigation of Possible Phenyl Participation in the Acetylenic Oxy-Cope Rearrangement.

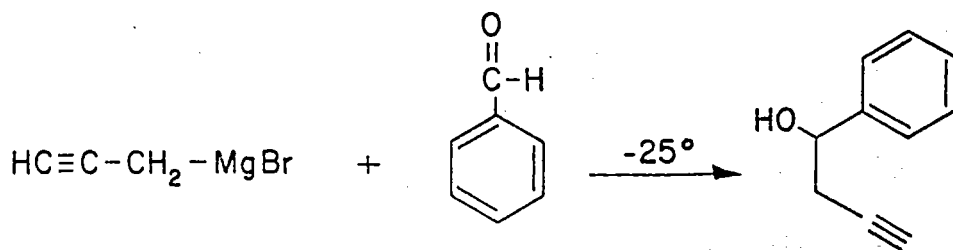
Glover⁵² thermolyzed 1-phenyl-3-buten-1-ol (77) and isolated benzaldehyde as the only condensed product.



No oxy-Cope rearrangement product could be detected. The kinetic parameters obtained for 5-hexen-1-yn-3-ol (63) suggested that triple bond participation lowers the activation energy required for the oxy-Cope process. Therefore attempts were made to observe phenyl participation for 1-phenyl-3-butyn-1-ol (76) and 1-phenyl-2-methyl-3-butyn-2-ol (78).

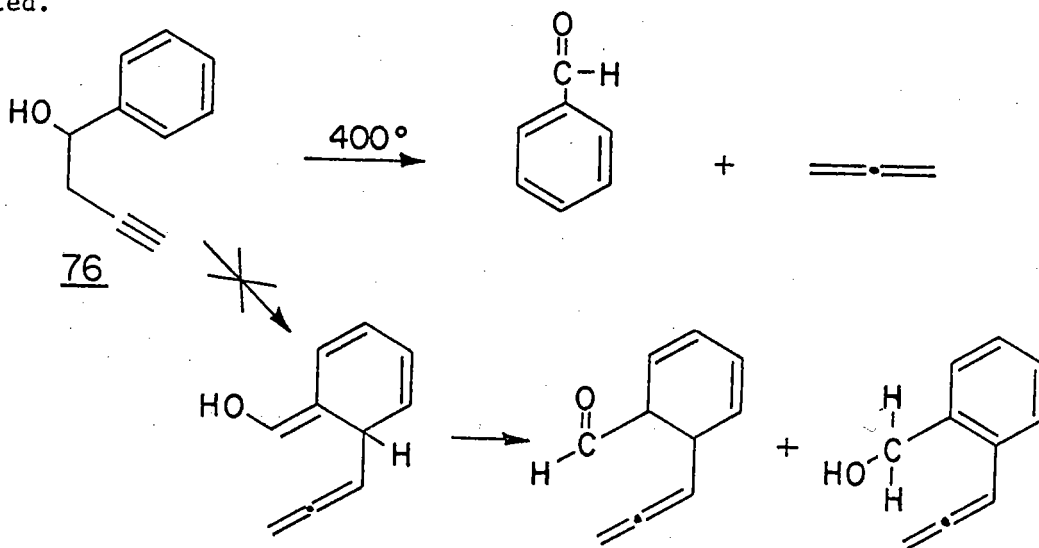


1-Phenyl-3-butyn-1-ol (76) was synthesized by the Grignard reaction of benzaldehyde with propargylmagnesium bromide, followed by hydrolysis.



The physical constants of 76 were in agreement with the literature⁶⁵ values and the infrared and n.m.r. spectra were consistent with the proposed structure. Hydrogenation of 76 gave phenyl n-propyl ketone as the major product, identified by its 2,4-dinitrophenylhydrazone derivative, which showed no melting point depression on admixture with authentic material.

Thermolysis of 76 produced benzaldehyde and a low boiling material believed to be allene. No trace of any oxy-Cope product could be detected.

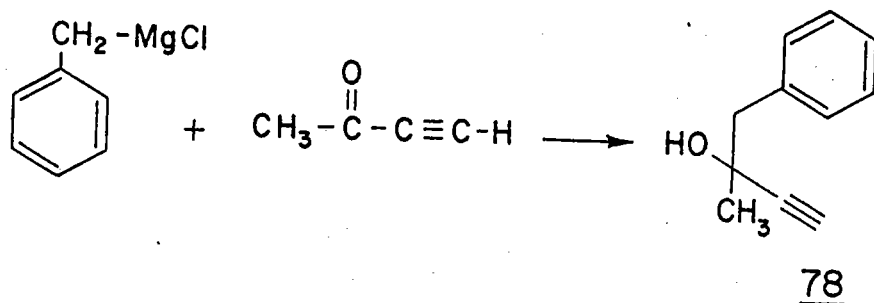


The benzaldehyde produced was identified by its characteristic odor, infrared spectrum and 2,4-dinitrophenylhydrazone derivative. The derivative showed no melting point depression on admixture with authentic material.

The absence of oxy-Cope rearrangements in these systems may be due to the fact that in the rearrangement pathway the aromatic ring must be attacked with resulting loss of aromatic resonance energy. Since the activation energy of the rearrangement pathway is greatly increased by this effect, the lower energy cleavage pathway dominates to the complete exclusion of the oxy-Cope pathway.

Another factor is that even if the oxy-Cope pathway possessed an activation energy sufficiently low to proceed at 400°, the resulting enol could restore the aromaticity of the benzene ring in the gas phase only via a symmetry forbidden 1,3 hydrogen shift. Therefore the reverse reaction, to give starting material, 76, would occur preferentially since this reaction restores the aromaticity in a symmetry allowed fashion.

1-Phenyl-2-methyl-3-butyn-2-ol (78), previously unreported, was prepared by the reaction of benzylmagnesium chloride with methyl ethynyl ketone.



The yield of 78 was low, but sufficient quantity was obtained for the following experimental work. The physical constants and elementary analysis of 78 were consistent with the proposed structure as were the infrared and n.m.r. spectra. They are detailed in the experimental section, page 156. Hydrogenation of 78 was quantitative and gave 1-phenyl-2-methyl-2-butanol, identified by comparison of its v.p.c. retention time and infrared spectrum with authentic material.

Thermolysis of 78, even at temperatures as high as 430°, gave only some low boiling fragmentation products and large quantities of unreacted material. No trace of any oxy-Cope product could be detected in the thermolyzed products. The reasons for the lack of any oxy-Cope rearrangement in this compound are probably similar to those discussed for the thermolysis of 1-phenyl-3-butyn-1-ol. In 78, the cleavage reaction also

would involve phenyl participation therefore both oxy-Cope and cleavage processes are unfavorable. In view of these results it would appear that phenyl participation in oxy-Cope or cleavage reactions is energetically an unfavorable process. The possibility remains, however, that phenyl participation in the oxy-Cope process could occur if a symmetry allowed 1,5 hydrogen transfer were possible to restore the aromatic system. Phenyl participation in the Cope rearrangement has been reported by Doering and Bragole⁶⁸ but under base catalysis where intermolecular hydrogen shifts can occur.

The above results are surprising since the Claisen rearrangement¹, which involves phenyl participation, is a facile process at 300 - 400°. The reasons for the comparative ease of the Claisen rearrangement are not within the scope of this thesis.

Preparation of 1-phenyl-3-butyn-1-ol (76)

To a 1 liter three neck flask, equipped with condenser, mechanical stirrer and dropping funnel, were added 24 g (1 mol) Mg turnings, 1 g propargyl bromide, 200 ml dry ether and 0.1 g of mercuric chloride. The mixture was warmed with stirring until a reaction commenced as evidenced by vigorous ether reflux. The flask was then immersed in a Dry Ice/acetone bath maintained at -20° , and a solution of 46 g redistilled propargyl bromide (total 0.4 mol) in 150 ml ether was added dropwise over a period of three hours while the bath temperature was maintained at -20° . After the addition was complete, a solution of 26 g redistilled benzaldehyde (0.25 mol) in 150 ml ether was added over a period of two hours, while the bath temperature was maintained between -10° and 0° . The mixture was allowed to reach room temperature and then was decomposed with ice/ammonium chloride. The ether and aqueous layers were separated and the aqueous layer extracted twice with 50 ml ether portions. The combined ether layers were washed twice with 25 ml water and were then dried with magnesium sulfate. The ether was evaporated, yielding a light yellow oil. Careful fractionation of the oil under reduced pressure yielded 28 g (77%) of material which proved to be v.p.c. homogeneous. B.p. 80° (0.5 mm), n_D^{26} 1.5457, d_4^{29} 1.0265, (lit.⁶⁵ b.p. 89° /1 mm, n_D^{20} 1.5470).

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.16; H, 6.90.
Found: C, 82.10; H, 6.92.

The infrared spectrum showed bands at 3400(s), 3300(spike), 3030(m), 2900(m), 2120(w), 1600(w), 1490(m), 1450(m), 1420(m), 1390(m), 1320(m), 1205(m), 1085(m), 1050(s), 1015(s), 945(m), 915(m), 865(m), 830(w), 775(m), 755(s), and 700(s) cm^{-1} .

The n.m.r. spectrum (δ scale) showed a triplet at 1.95 (1H, acetylenic), a doublet of doublets at 2.50 (2H, aliphatic), a broad singlet at 3.50 (1H, hydroxyl), a triplet at 4.70 (1H, methine), and a singlet at 7.25 (5H, phenyl).

Hydrogenation of 1-phenyl-3-butyn-1-ol.

A 1.04 g (7.1 mmols) sample of the alcohol in pentane, over Pd/C, was found to absorb 365 ml of hydrogen at 298° K, which corresponded to 105% of the 347 ml theoretically required to saturate a triple bond. After filtering off the catalyst and evaporating the pentane, the product was analyzed by v.p.c. and found to consist of a major product of 95% purity. The v.p.c. retention time and infrared spectrum of the hydrogenated alcohol were identical to those of an authentic sample of 1-phenyl-1-butanol, prepared by the action of a n-propyl magnesium bromide on benzaldehyde by standard procedures. Dichromate oxidation of the hydrogenated alcohol gave a ketone whose 2,4-dinitrophenylhydrazone was prepared by the Shriner and Fuson⁶⁰ procedure. Recrystallization from ethanol gave orange red crystals, m.p. 189-91° (lit.:m.p.⁶² 190°) which showed no melting point depression on admixture with an authentic sample. The authentic derivative was prepared from

n-propyl phenyl ketone obtained by dichromate oxidation of the above authentic alcohol.

Vapor phase thermolyses of 1-phenyl-3-butyn-1-ol (76)

This compound was thermolyzed at temperatures from 370° to 430°. V.p.c. analyses of the thermolyzed products always showed a very low boiling constituent, believed to be allene, and a single higher boiling constituent, shown to be benzaldehyde, resulting from the cleavage reaction. No traces of any component resulting from an oxy-Cope rearrangement could be detected in the thermolyses products even when large injections and high sensitivities were employed with the analytical gas chromatograph.

In a typical experiment, 12.16 g of the alcohol was passed through the thermolysis column at a temperature of 430-5°, a pressure of 10 mm, and a drop rate of three drops per minute. The condensed product, 8.69 g (72% recovery), was analyzed by v.p.c. and found to consist of 3% of a very low boiling constituent, believed to be allene, and 97% high boiling constituent shown to be benzaldehyde as follows.

The cleavage product was obtained nearly pure from the thermolysis. After bubbling nitrogen through the product to remove the suspected allene, the material was easily identified by its characteristic odor, v.p.c. retention time and infrared spectrum superimposable on that of authentic redistilled benzaldehyde.

The thermolysis product was converted to its 2,4-dinitrophenyl-

hydrazone by the method of Shriner and Fuson.⁶⁰ Recrystallization from ethyl acetate yielded orange crystals, m.p. 238-40° (lit.⁶⁰ 237°) which showed no melting point depression on admixture with an authentic sample.

Preparation of 1-phenyl-2-methyl-3-butyn-2-ol (78)

This compound, previously unreported, was prepared by the addition of an ethereal solution of methyl ethynyl ketone to benzylmagnesium chloride.

In a 2-liter three neck flask, equipped with mechanical stirrer, dropping funnel and condenser, were placed 48 g (2 mols) magnesium turnings, 400 ml dry ether and several iodine crystals. Then 10 ml of a solution of 102 g (0.8 mol) redistilled benzyl chloride in 200 ml ether was added directly to the solution. After five minutes a reaction commenced as evidenced by vigorous boiling. The stirrer was started and the remainder of the benzyl chloride was added dropwise over a period of six hours. The solution was stirred for one hour and then a solution of 37 g (0.55 mol) redistilled methyl ethynyl ketone in 100 ml dry ether was added, dropwise, over a period of two hours. After stirring for one half hour the mixture was decomposed with ice/ammonium chloride. The aqueous layer was extracted with two 150 ml ether portions and the combined ether extracts washed four times with 100 ml portions of water, dried with magnesium sulfate and the ether was evaporated. The remaining thick brown oil was flash distilled under reduced pressure

to remove non-volatile material. Careful fractionation under reduced pressure yielded 8.40 g (10%) of pure material, b.p. 94-96° (4 mm), n_D^{23} 1.5320.

<u>Anal.</u>	Calcd. for $C_{11}H_{12}O$:	C, 82.47;	H, 7.55.
	Found:	C, 82.59;	H, 7.48.

The infrared spectrum showed bands at 3400(s), 3300(spike), 3030(m), 2990(m), 2940(m), 2120(w), 1610(w), 1500(s), 1460(s), 1380(s), 1360(s), 1290(m), 1240(m), 1160(s), 1120(s), 1090(s), 1060(s), 1035(m), 935(s), 875(m), 760(m) and 700(s) cm^{-1} .

The n.m.r. spectrum (δ scale) showed a singlet at 1.50 (3H, methyl), a broad singlet overlapping another singlet at 2.45 (2H, acetylenic and hydroxyl protons) which collapses to a singlet (1H, acetylenic) on addition of D_2O , a singlet at 2.95 (2H, benzylic) and a singlet at 7.3 (5H, phenyl).

Hydrogenation of 1-phenyl-2-methyl-3-butyne-2-ol

A 0.854 g (5.34 mmols) sample of the alcohol in methanol, over Pd/C absorbed 265 ml of hydrogen, at 297°K, which corresponded to 102% of the theoretical quantity for saturating a triple bond. The product was identified as 1-phenyl-2-methyl-2-butanol by comparison of v.p.c. retention time and infrared spectrum with authentic material. The authentic material was synthesized by the reaction of benzylmagnesium chloride with 2-butanone followed by hydrolysis.

Vapor phase thermolyses of 1-phenyl-2-methyl-3-butyn-2-ol (78)

This compound was thermolyzed at temperatures from 370° to 410° and at various pressures. The product, usually representing a recovery of 85-90% was analyzed by v.p.c. and found to consist of some low boiling fragmentation products and large quantities of unreacted starting material. The amount of fragmentation products, which were not identified, increased with increasing temperature or residence time but never exceeded 25% of the recovered product. No trace of any oxy-Cope product could be detected in the thermolysis mixture. The recovered starting material was identified by its v.p.c. retention time and its infrared spectrum.

In a typical experiment, 1.81 g of the alcohol was thermolyzed at 410-15° and a pressure of 22 mm. A drop rate of four drops/minute was employed. The recovered product weighed 1.55 g (86% recovery). V.p.c. analysis indicated the thermolysis product to consist of 25% low boiling fragmentation products and 75% unreacted starting alcohol.

In an attempted liquid phase Cope rearrangement of this alcohol, 1.37 g was heated in a distilling flask for 30 hours at 210°. The product was dark brown and polymeric. V.p.c. indicated the only volatile product to be unreacted starting alcohol.