

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

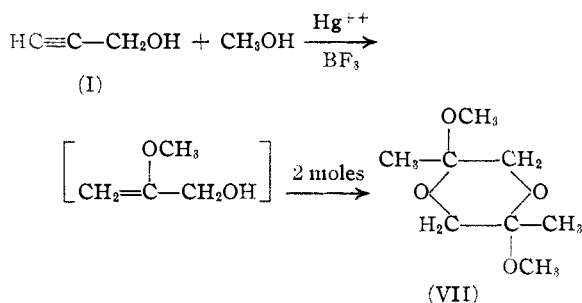
Catalytic Addition Reactions of Acetylenic Alcohols^{1,2}

BY G. F. HENNION AND W. S. MURRAY

Introduction

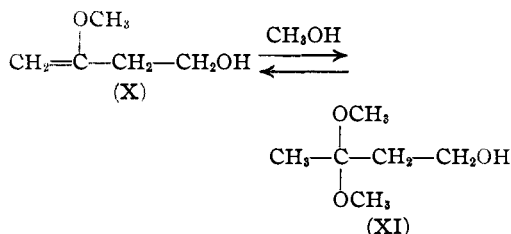
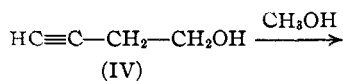
A previous paper³ in this series describes the reactions of dimethylethynealcohol with methanol and acetic acid catalyzed by mercuric oxide and boron fluoride. The results of this investigation indicated the desirability of a more extensive study of analogous reactions. The products formed by the addition of methanol, ethylene glycol and acetic acid to a number of representative acetylenic alcohols have now been determined. The alcohols used (Table I) were prepared by the condensation of the appropriate aldehyde or ketone with sodium acetylide in liquid ammonia.^{3,4}

Propargyl alcohol (I) with methanol yielded only 2,5-dimethoxy-2,5-dimethyl-1,4-dioxane (VII), obviously by methanol addition and bimolecular condensation.



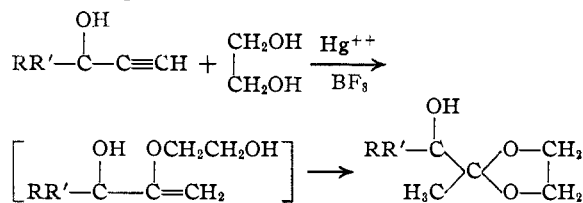
In a similar manner methylethynealcohol (II) and phenylethynealcohol (III) gave 2,5-dimethoxy-2,3,5,6-tetramethyl-1,4-dioxane (VIII), and 2,5-dimethoxy-2,5-dimethyl-3,6-diphenyl-1,4-dioxane (IX), respectively.

β -Ethynealcohol (IV) cannot undergo these bimolecular condensations and so gave principally the vinyl ether (X) and the ketone acetal (XI).

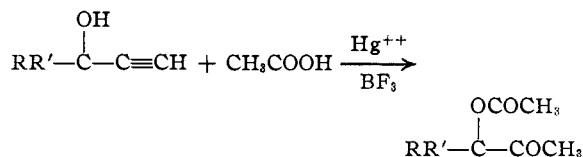


The latter (XI) is unstable and upon distillation reverts considerably to (X). In fact it was not possible to obtain (XI) in analytically pure form. 1-Ethynealcohol (VI) yielded only an intractable mixture which appeared to contain both methanol addition products and other compounds.

Ethylene glycol added to the ethynealcohols (II, V and VI) in identical manner to produce the corresponding dioxolanes, namely, 2-methyl-2-(1-hydroxyethyl)-1,3-dioxolane (XII), 2-methyl-2-(2-hydroxyisopropyl)-1,3-dioxolane (XIII), and 2-methyl-2-(1-hydroxycyclohexyl)-1,3-dioxolane (XIV). Thus ring closure through the glycol occurs in preference to bimolecular condensation.



The ethynealcohols reacted with acetic acid by esterification and triple bond hydration as follows.



The four acyloin derivatives, acetol acetate (XV), acetoin acetate (XVI), phenylacetylalcohol acetate (XVII), and 1-acetylcyclohexanol acetate (XVIII) were prepared in this manner. As in the methanol and glycol reactions, β -ethynealcohol gave an unstable product with acetic acid. In this respect β -ethynealcohol differs from the ethynealcohols.

The substituted dioxanes from the methanol reactions, the glycol addition compounds, and the

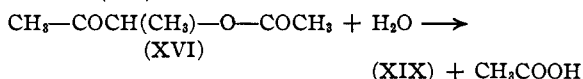
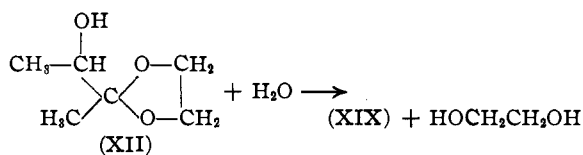
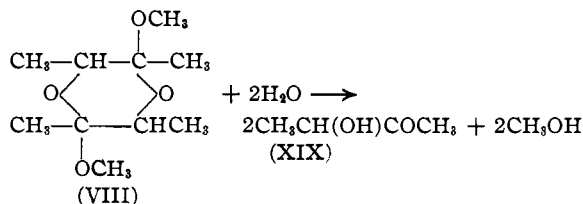
(1) Paper XLIV on substituted acetylenes and their derivatives; previous paper, *THIS JOURNAL*, **63**, 2683 (1941).

(2) After this paper was written, it was noted that some similar studies have been reported by I. N. Nazarov, *Bull. acad. sci. U. R. S. S., Classe sci. chim.*, 195-202 (1940); *C. A.*, **36**, 742-46 (1942). However this work was concerned only with dimethylethynealcohol. Using the technique developed in this Laboratory, he prepared a variety of compounds, including some previously reported.⁴

(3) Froning and Hennion, *THIS JOURNAL*, **62**, 653 (1940).

(4) Campbell, Campbell and Eby, *ibid.*, **60**, 2882 (1938).

acyloin acetates hydrolyze in acid solution to the corresponding acyloin as shown below for the methylethynylcarbinol products.



The five possible acyloins were thus prepared from the various condensation products and the semicarbazone melting points observed to be in agreement with the literature values. Physical constants and analyses are given in Table II.

TABLE I
ACETYLENIC ALCOHOLS

Alcohol	B. p. °C.	Mm.	n_D^{20}	d_4^{20}	Yield, %
(I) HC≡CCH ₂ OH	54	57	1.4310	0.9715	10
(II) HC≡CCH(CH ₃)OH	46	50	1.4256	0.8948	61
(III) HC≡CCH(C ₆ H ₅)OH	80	4	1.5505	1.0655	58
(IV) HC≡CCH ₂ CH ₂ OH	50	28	1.4410	0.9260	65
(V) HC≡CC(CH ₃) ₂ OH	104	760	1.4211	0.8623	77
(VI) HC≡CC ₆ H ₁₀ OH ^{a,b}	68	11	1.4826		87

^a 1-Ethynylcyclohexanol. ^b M. p. 32°.

TABLE II

YIELDS, CONSTANTS AND ANALYTICAL DATA FOR PRODUCTS

Compound	B. p.		n_D^{20}	d_4^{20}	MR		Yield, %	Formula	Mol. wt.		Carbon, %		Hydrogen, %	
	°C.	Mm.			Calcd.	Obsd.			Calcd.	Obsd.	Calcd.	Obsd.	Calcd.	Obsd.
3-Methoxy-3-butanol-1	45.5	20	1.4164	0.9284	27.99	27.63	47	C ₆ H ₁₀ O ₂	102	99				
3,3-Dimethoxy-1-butanol	54-6	5	1.4372	1.0140	34.72	34.62	10	C ₆ H ₁₄ O ₂	134	127				
1,4-Dioxane														
2,5-Dimethoxy-2,5-dimethyl- ^a							5	C ₈ H ₁₆ O ₄	176	178	54.53	54.33	9.15	9.23
2,5-Dimethoxy-2,3,5,6-tetramethyl- ^b							41	C ₁₀ H ₂₀ O ₄	204	201				
2,5-Dimethoxy-2,5-dimethyl-3,6-diphenyl- ^c							36	C ₂₈ H ₂₄ O ₄	328	337	73.13	73.13	7.37	7.67
1,3-Dioxolane														
2-Methyl-2-(1-hydroxyethyl)-	69	11	1.4405	1.0875	32.52	31.94	67	C ₆ H ₁₂ O ₃	132	134	54.54	54.18	9.16	9.16
2-Methyl-2-(2-hydroxyisopropyl)-	70	12	1.4416	1.0600	37.14	36.42	57	C ₇ H ₁₄ O ₃	146	149	57.50	57.54	9.66	9.95
2-Methyl-2-(1-hydroxycyclohexyl)- ^d							63	C ₁₀ H ₁₈ O ₃	186	184	64.49	64.44	9.74	9.66
Acetate														
Acetol-	65	11	1.4141	1.0757	26.95	27.11	30	C ₆ H ₈ O ₂						
Acetoin-	56	10	1.4129	1.0258	31.58	31.69	41	C ₆ H ₁₀ O ₂						
Phenylacetylcarbinol-	134	10	1.5081	1.1116	51.32	51.06	50	C ₁₁ H ₁₂ O ₂	192	187	68.73	68.10	6.30	6.38
1-Acetylcyclohexanol-	109	11	1.4591	1.0555	47.85	47.71	35	C ₁₀ H ₁₈ O ₂	184	180	65.20	64.96	8.76	8.81

^a M. p. 125°. ^b M. p. 77°; % CH₃O, calcd. 30.2; obsd. 29.8. ^c M. p. 254-256°. ^d M. p. 56°.

Experimental

Acetylenic Alcohols.—These were obtained as previously described.^{3,4} Propargyl alcohol was prepared from paraformaldehyde by addition of an ether slurry to sodium

acetylide in liquid ammonia. Ethylene oxide was used to prepare β-ethynylethanol.

Reactions with Methanol.—The catalyst was prepared by heating together for a few minutes 5 g. of red mercuric oxide, 2 ml. of ether-boron fluoride, 2 ml. of methanol and a few crystals of trichloroacetic acid. A liter three-neck flask provided with a reflux condenser, mechanical stirrer and dropping funnel was used. For a mole of acetylenic alcohol, two moles of reagent grade methanol was added to the catalyst and heated to 45°. Two moles of methanol was mixed with the acetylenic alcohol and the solution added dropwise to the catalytic mixture within an hour. The temperature was held between 45 and 55° by occasional cooling. After an additional hour of stirring the mixture was cooled, neutralized with 10 g. of anhydrous potassium carbonate and centrifuged. The supernatant liquid was decanted and the excess methanol removed by distillation. Compounds (X) and (XI) were recovered by fractional distillation. The solids (VII, VIII and IX) were collected by filtration from the distillation residues and purified by crystallization, usually from dilute methanol. In the case of (IX) it was necessary to crystallize from nitrobenzene or pyridine.

Reactions with Acetic Acid.—The catalyst was prepared as described above. A mixture of one mole each of acetic acid and acetylenic alcohol was added dropwise to the solution of the catalyst in one mole of acetic acid. The temperature was held between 55 and 65°. The product was neutralized with saturated sodium carbonate solution and extracted with ether. The organic layer was dried over potassium carbonate, the ether removed by distillation and the residue fractionated.

Reactions with Ethylene Glycol.—A suspension of the usual catalytic mixture in one mole of ethylene glycol was heated to 65°. This was followed by the dropwise addition of a mixture of 0.5 mole of glycol and one mole of acetylenic alcohol. After an interval of stirring, the catalyst was

neutralized with potassium carbonate and the mixture centrifuged. The supernatant liquid was then distilled.

Hydrolysis to Acyloins.—One gram of 2,5-dimethoxy-2,5-dimethyl-1,4-dioxane was dissolved in 10 ml. of dilute

alcohol containing a few drops of concentrated hydrochloric acid. The solution was heated for fifteen minutes, cooled, neutralized with sodium carbonate, and the semicarbazone prepared *in situ* in the usual manner; m. p. 190–191°; literature, 192°.⁵ Other acyloin semicarbazone melting points were as follows: from (VIII) and (XII), 184–186°; from (IX) and (XVII), 193°; from (XIII), 161–162°; from (XIV) and (XVIII), 202–203°.

(5) Hoogenen and Jansen, *Rec. trav. chim.*, **51**, 260 (1932).

Summary

1. Acetylenic carbinols have been condensed with methanol to produce a number of substituted dioxanes and with ethylene glycol to form various dioxolanes.

2. Similar reactions with acetic acid yield acyloin acetates.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Keto Ethers. IX. Propoxymethyl Alkyl (or Phenyl) Ketones¹

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During the past decade much attention has been directed in this Laboratory to a study of bifunctional compounds. The keto ethers have proved to be of special interest because of their value as intermediates in further synthesis, for example, of 5,5-disubstituted hydantoins and substituted cinchoninic acids. The latter contain structures favorable to exhibition of pharmacological activities of widely varying types.

In the present study the two isomeric chloromethyl propyl ethers have been prepared and converted into the corresponding propoxyacetone nitriles. The latter, in turn, have been caused to react with suitable Grignard reagents to yield fourteen new examples of *n*- or isopropoxymethyl alkyl ketones and of two analogous phenyl ketones.

Experimental

Chloromethyl Propyl Ethers.—Three moles (180 g.) of *n*-propyl alcohol and one equivalent (90 g.) of trioxymethylene were mixed, cooled, and saturated with dry hydrogen chloride during a period of four hours; during the reaction the trioxymethylene dissolved slowly and two layers formed. The upper, ethereal layer was separated, dried and fractionated; yield, 210 g. (64%) of chloromethyl *n*-propyl ether³ boiling at 26–28° (32 mm.), 110° (755 mm.), n_D^{20} 1.4106, d_4^{20} , 0.9894, *MR* calcd. 27.18, *MR* found 27.21. The chloro ether was prepared also in about 60% yield from commercial formalin solution. This chloro ether is very susceptible to hydrolysis and should be used as quickly as possible in further synthesis.

Anal. Calcd. for C₃H₇ClO: Cl, 32.66. Found: Cl, 32.95.

(1) Previous paper in this series, Henze and Wilson, *This Journal*, **63**, 2112 (1941).

(2) Constructed in part from the M.A. theses of the four junior collaborators.

(3) L. Henry, *Bull. soc. chim.*, [2] **44**, 458 (1835); Favre, *ibid.*, [3] **11**, 1095 (1894); Karvonen, *Am. Acad. sci. Fennicae*, **A3**, 1 (1941).

For the preparation of the isopropyl analog, 540 g. (9 moles) of isopropyl alcohol and 750 g. of 36% formalin solution (equivalent to 9 moles of formaldehyde) were utilized. There was obtained 480 g. (49% yield) of isopropyl chloromethyl ether⁴ boiling at 36° (45 mm.), 101° (750 mm.), n_D^{20} 1.4095, d_4^{20} , 0.9843, *MR* calcd. 27.18, *MR* found 27.30.

Anal. Calcd. for C₃H₇ClO: Cl, 32.66. Found: Cl, 33.01.

The chloro ethers are relatively unstable, especially upon exposure to atmospheric moisture, and were converted at once into the corresponding nitriles.

Propoxyacetone nitriles.—By heating a well-stirred mixture of 230 g. of dry cuprous cyanide and an equal volume of anhydrous ether to gentle refluxing and slowly adding 212 g. of chloromethyl *n*-propyl ether, diluted with an equal volume of ether, through a period of two hours, filtering from cuprous salts, and fractionation there was obtained 164 g. (55% yield) of *n*-propoxyacetone nitrile boiling at 56° (40 mm.), 152° (751 mm.), n_D^{20} 1.4001, d_4^{20} , 0.8971, *MR* calcd. 26.75, *MR* found 26.75.

Anal. Calcd. for C₃H₇NO: N, 14.13. Found: N, 13.99.

Isopropoxyacetone nitrile was obtained in 56% yield from interaction of 480 g. of chloromethyl isopropyl ether and 520 g. of dry cuprous chloride suspended in 1000 g. of anhydrous ether; b. p. 74° (53 mm.), 145–146° (748 mm.); n_D^{20} 1.3960, d_4^{20} , 0.8918, *MR* calcd. 26.75, *MR* found, 26.69.

Anal. Calcd. for C₃H₇NO: N, 14.13. Found: N, 13.93.

Preparation of Keto Ethers.—The appropriate Grignard reagent, prepared in the usual manner from an alkyl or phenyl halide, was treated with slightly less than the equivalent amount of a propoxyacetone nitrile (using 0.4 to 1.0 molar quantities); usually reaction was vigorous and more ether had to be added to permit stirring of the

(4) Litterschied, *Ann.*, **330**, 108 (1903); Stappers, *Chem. Zentr.*, **76**, 921 (1905); Farren, Fife, Clark and Garland, [*This Journal*, **47**, 2419 (1925)] reported n_D^{20} 1.4592, d_4^{20} , 0.9790, *MR* obs. 26.85. Actually, from this index of refraction, the calculated *MR* is 30.33, whereas an index of refraction of 1.3994 is required to yield the calculated *MR* of 26.85.