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

Reactions of Dialkoxyalkanes with Alkynylmagnesium Bromides[1]

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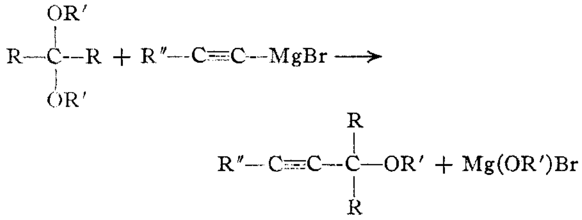
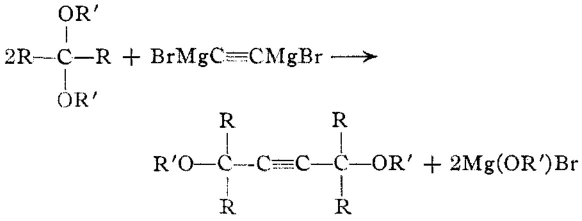
Introduction

It has been shown by Spaeth[2] and by Tschitschibabin and Jelgasin[3] that several common acetals react with certain alkyl- and arylmagnesium halides to yield various amounts of ethers through replacement of one alkoxyl group by the hydrocarbon radical. This reaction has been applied in the present research by utilizing the acetylenic magnesium bromides and acetal-type compounds for the synthesis of alkyl ethers of alkynyl carbinols and glycols, according to the following type equations, in which (R') and (R'') represent alkyl groups and (R) may be an alkyl radical or hydrogen atom



$$\mathrm{R-\overset{OR'}{\underset{OR'}{C}}-R + R''-C\equiv C-MgBr \longrightarrow R''-C\equiv C-\overset{R}{\underset{R}{C}}-OR' + Mg(OR')Br}$$



$$\mathrm{2R-\overset{OR'}{\underset{OR'}{C}}-R + BrMgC\equiv CMgBr \longrightarrow R'O-\overset{R}{\underset{R}{C}}-C\equiv C-\overset{R}{\underset{R}{C}}-OR' + 2Mg(OR')Br}$$

Several ethers of acetylenic glycols as well as certain methoxybutynes have been prepared previously by the action of halomagnesium or sodium compounds of acetylenes on various haloethers, as shown below[4-7]

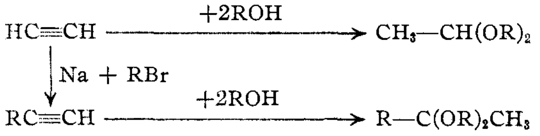
$$\mathrm{CH_3OCH_2Cl + BrMgC\equiv C-CH_3 \longrightarrow CH_3OCH_2-C\equiv C-CH_3 + MgBrCl}$$

$$\mathrm{CH_3OCH_2CH_2Br + NaC\equiv CH \longrightarrow CH_3OCH_2CH_2-C\equiv CH + NaBr}$$

$$\mathrm{2ROCH_2Cl + BrMgC\equiv CMgBr \longrightarrow ROCH_2C\equiv CCH_2OR + 2MgClBr}$$

By treating propargylic acetal, obtained from acrolein, with methyl-, ethyl- and phenylmagnesium bromides, Grard[8] prepared the corresponding 3-ethoxy-1-alkynes. The methyl ethers of some acetylenic carbinols also have been synthesized from methyl sulfate and the sodium alcoholates.[9]

The object of this investigation was to study the reactivity of different types of dialkoxyalkanes toward acetylenic Grignard reagents, and to determine the practicability of the reaction as a general method for the synthesis of various classes of acetylenic ethers. The method lends itself particularly well since the intermediate acetals and ketals are readily prepared directly from acetylene and the alkylacetylenes



$$\begin{tikzcd} \mathrm{HC\equiv CH} \arrow[r, "+2\mathrm{ROH}"] \arrow[d, "\mathrm{Na + RBr}"] & \mathrm{CH_3-CH(OR)_2} \\ \mathrm{RC\equiv CH} \arrow[r, "+2\mathrm{ROH}"] & \mathrm{R-C(OR)_2CH_3} \end{tikzcd}$$

The reactions carried out are listed in Table I, along with the physical constants of the acetylenic ethers obtained. Table II shows the analysis of the ethers not reported in the literature. All compounds distilled as water-white liquids having very pleasant odors.

Experimental

Reagents.—1-Hexyne and 1-heptyne were prepared by a modification of the Picon synthesis.[10] Ethyl orthoformate was synthesized according to the method described in the literature.[11] Ethylal and *n*-propylal were Eastman Kodak Company products, and were purified by distillation before use.

Preparation of 1,1- and 2,2-Dialkoxyalkanes.—1,1-Diethoxyethane and 2,2-dimethoxyhexane were obtained by the addition of ethanol and methanol to acetylene[12] and to 1-hexyne,[13] respectively, by means of a mercuric oxide-boron trifluoride catalyst.

The preparation of 1,1-diethoxypropane was effected by the addition of an ether solution of 1.0 mole ethylmagnesium bromide to a solution of 222 g. (1.50 moles) of ethyl orthoformate in dry ether. The method employed was similar to the general procedure described below. Special precautions were taken, however, to use an excess of ester to ensure reaction of only one alkoxyl group. Hy-

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[1] Paper XXVII on the chemistry of the alkylacetylenes and their derivatives; previous paper, THIS JOURNAL, **60**, 1711 (1938).

[2] Spaeth, *Monatsh.*, **35**, 330, 463 (1914).

[3] Tschitschibabin and Jelgasin, *Ber.*, **47**, 48, 1843 (1914).

[4] Yvon, *Compt. rend.*, **180**, 748 (1925).

[5] Lespieau, *ibid.*, **144**, 1161 (1907); **194**, 287 (1932).

[6] Kroeger and McCusker, THIS JOURNAL, **59**, 213 (1937).

[7] Gauthier, *Ann. chim. phys.*, [8] **16**, 334 (1909).

[8] Grard, *Ann. chim.*, **13**, 336–383 (1930).

[9] Gredy, *Compt. rend.*, **198**, 2254 (1934).

[10] Vaughn, Hennion, *et al.*, *J. Org. Chem.*, **2**, 1 (1937).

[11] "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 253.

[12] Hinton and Nieuwland, THIS JOURNAL, **52**, 2892 (1930).

[13] Killian, Hennion and Nieuwland, *ibid.*, **56**, 1384 (1934).

TABLE I

DIALKOXYALKANES WITH ALKYNYLMAGNESIUM BROMIDES

No.	Dialkoxyalkane	RMgBr R—	Ether Formula	B. p., °C.	Mm.	d^{25}_4	$n^{25}D$	MR Calcd.	MR Obsd.
1	$H_2C(OC_2H_5)_2$	$C_4H_9C{\equiv}C—$	$C_4H_9C{\equiv}CCH_2(OC_2H_5)$	90	24	0.8530	1.4391	43.41	43.12
2	$H_2C(OC_3H_7)_2$	$C_4H_9C{\equiv}C—$	$C_4H_9C{\equiv}CCH_2(OC_3H_7)$	61	4	.8315	1.4340	48.03	48.20
3	$CH_3CH(OC_2H_5)_2$	$C_5H_{11}C{\equiv}C—$	$C_5H_{11}C{\equiv}CCHCH_3(OC_2H_5)$	108	40	.8144	1.4302	52.65	53.38
4	$C_2H_5CH(OC_2H_5)_2$	$C_4H_9C{\equiv}C—$	$C_4H_9C{\equiv}CCHC_2H_5(OC_2H_5)$	105	25	.8290	1.4335	52.65	52.70
5	$C_6H_5CH(OC_2H_5)_2$	$C_4H_9C{\equiv}C—$	$C_4H_9C{\equiv}CCHC_6H_5(OC_2H_5)$	115	4	.9406	1.5033	67.51	67.97
6	$C_4H_9C{\equiv}CCH—C_2H_5(OC_2H_5)$	$C_4H_9C{\equiv}C—$	$(C_4H_9C{\equiv}C)_2CH(OC_2H_5)$	121	4	.8550	1.4505	69.12	69.24
7	$C_4H_9C{\equiv}C—CH(OC_2H_5)_2$	$C_4H_9C{\equiv}C—$	$C_4H_9C{\equiv}CC(C_4H_9)CH_2(OCH_3)$	83	4	.8191	1.4412	63.25	63.13
8	$CH_3OC_2H_4OCH_3$	$C_4H_9C{\equiv}C—$	$C_4H_9C{\equiv}CC_2H_4OCH_3$	91	30	.8285	1.4317	43.41	43.68
9	$CH_3CH(OC_2H_5)_2$	$HC{\equiv}C—$	$HC{\equiv}C—CH(OC_2H_5)CH_3$	88	750	.7986	1.4009	29.01	29.71
10	$C_6H_5CH(OC_2H_5)_2$	$HC{\equiv}C—$	$HC{\equiv}C—CH(OC_2H_5)C_6H_5$	103	15	1.0425	1.5328	47.96	47.58
11	$CH_3CH(OC_2H_5)_2$	$—C{\equiv}C—$	$CH_3CH(OC_2H_5)C{\equiv}CCH(OC_2H_5)CH_3$	179	730	0.8929	1.4328	49.67	49.53
12	$H_2C(OC_3H_7)_2$	$—C{\equiv}C—$	$C_3H_7OCH_2C{\equiv}CCH_2(OC_3H_7)$	150	20	.8892	1.4322	49.67	49.60

TABLE II

ANALYSES OF NEW ACETYLENIC ETHERS

No.	Empirical formula	Mol. wt.[a] Calcd.	Mol. wt.[a] Obsd.	% Alkoxyl[b] Calcd.	% Alkoxyl[b] Obsd.
1	$C_9H_{16}O$	140	142	32.11	31.24
2	$C_{10}H_{18}O$	154	153	...	...[c]
3	$C_{11}H_{20}O$	168	167	26.76	25.85
4	$C_{11}H_{20}O$	168	165	26.76	25.79
5	$C_{15}H_{20}O$	216	219	20.83	20.04
6	$C_{16}H_{24}O$	220	221	20.45	19.42
7	$C_{13}H_{24}O$	196	198	15.81	16.36
8	$C_9H_{16}O$	140	138	22.13	21.54

[a] Cryoscopic in benzene. [b] Zeisel method. [c] *Anal.* Calcd. for $C_{10}H_{18}O$: C, 77.92. Found: C, 77.17. (By wet combustion method.)

drolysis was carried out by the careful addition of dilute acetic acid, and the product was neutralized immediately to minimize conversion to the aldehyde. The yield amounted to 100 g. (75% of the theoretical), b. p. 122–123°.

Ethyl orthoformate, treated in a similar manner with phenylmagnesium bromide, gave a 55% yield of benzylidene acetal, b. p. 92–93° at 10 mm.

1,1-Diethoxy-2-heptyne (not previously reported) was obtained analogously, utilizing hexynylmagnesium bromide. The yield was 69%, b. p. 97–98° at 10 mm.; $n^{27}D$ 1.4320; d^{25}_4 0.8668.

Preparation of 1,2-Dimethoxyethane.—A modification of the reported method[14] was employed, which resulted in increased yields and a purer product.

Seventeen grams (0.75 mole) of metallic sodium was added in small portions to 228 g. (3.0 moles) of ethylene glycol monomethyl ether (Methyl Cellosolve) after which 94.5 g. (0.75 mole) of methyl sulfate was added dropwise, with stirring, during thirty minutes. After heating for an additional fifteen minutes at 85–90° on an oil-bath, the product was distilled through a short Vigreux column. All material boiling below 100° was collected and this fraction redistilled. The amount of product boiling at 82–83° was 54.5 g. (81% yield).

Reaction of Dialkoxyalkanes with Hexynylmagnesium Bromide.—The following represents the general procedure employed for all reactions.

Ethylmagnesium bromide was prepared in the usual manner, using 12 g. (0.50 mole) of magnesium turnings in anhydrous ether, and sufficient ethyl bromide to react with all the metal. To this solution was added dropwise and with stirring 41 g. (0.50 mole) of 1-hexyne, diluted with an equal volume of dry ether. The reaction mixture was allowed to stand for twelve hours, and was then stirred and refluxed vigorously for two hours longer. After allowing to cool, this solution was transferred to a dropping funnel and added slowly to 0.55 mole of the dialkoxyalkane dissolved in 100 cc. of anhydrous ether. The 1-liter, 3-necked flask used for preparation of the Grignard reagent was employed and constant agitation was effected by means of a sealed mechanical stirrer. Throughout the addition the reaction mixture was kept at a temperature sufficiently high, by heating on a water-bath, to distil off the ether at a constant rate. It was found advantageous to add the Grignard reagent through a short, upright water-cooled condenser to prevent evaporation of the ether and solidification in the funnel stem. Stirring was continued for one hour with the water-bath at 95°, after which the semi-solid mixture was hydrolyzed in the cold with dilute hydrochloric acid. The organic layer was dried and distilled under reduced pressure. It was found that merely refluxing the reactants in dry ether with stirring for two to three hours gave lower yields of acetylenic ether than those obtained by removing the ether continuously and heating as described above.

In the reaction involving 1,2-dimethoxyethane, the reaction mixture was heated on a near-boiling water-bath for three hours after the ether had been removed. The remainder of the procedure was the same as that given.

Reaction of Dialkoxyalkanes with Ethynylmagnesium Bromides.—Acetylene dimagnesium bromide was obtained by bubbling acetylene gas, purified by passing through concentrated sulfuric acid and a calcium chloride tower, through a solution of ethylmagnesium bromide in anhydrous ether during the course of eight to ten hours with constant stirring. After refluxing to remove ethane and excess acetylene, the Grignard reagent was added to twice its molal quantity of dialkoxyalkane in the usual manner. In addition to the ethers shown in Table I, 0.50 mole of the reagent, when treated with ethyl orthoformate, gave 69 g. of the diacetal, 1,1,4,4-tetraethoxy-2-butyne, b. p. 107° at 4 mm.; $n^{30}D$ 1.4315; d^{22}_4 0.9525.

By adding bromobenzene to magnesium turnings in dry ether and simultaneously passing acetylene gas into the solution, as above, with vigorous refluxing, a Grignard reagent was obtained which, by its reactions with acetals proved to be mainly ethynylmonomagnesium bromide.

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[14] Clarke, *J. Chem. Soc.*, **101**, 1802 (1912).

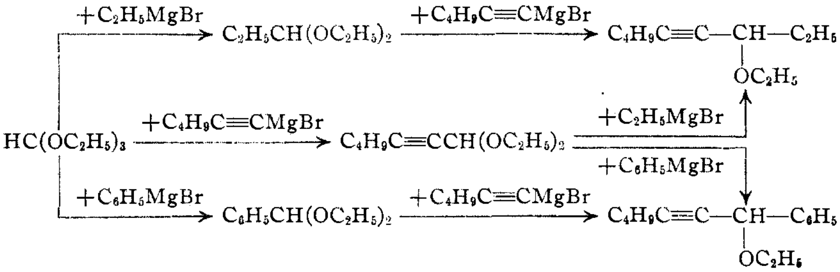
With orthoformic ester. 0.50 mole of the reagent gave 24 g. of the monoacetal, 3,3-diethoxy-1-propyne, b. p. 35° at 10 mm.; n^{22}_{D} 1.4139; d^{22}_{4} 0.8942.

Reaction of 1,1-Diethoxyethane with Sodium Acetylides.—Ninety-six grams (1.0 mole) of 1-heptyne was added slowly to a solution of approximately 1.0 mole of sodamide in liquid ammonia. When most of the ammonia had evaporated, the solid acetylide was suspended in 600 cc. of anhydrous ether. To this solution was added 147 g. (1.25 moles) of ethyl acetal and the mixture refluxed with stirring for two hours. After hydrolysis the organic layer was purified, and distillation yielded 7 g. of 2-ethoxy-3-nonyne, b. p. 108° at 40 mm.

Since liquid ammonia was found to be an excellent solvent for ethyl acetal, the reaction with sodium amyl acetylide was carried out in this medium as well as in *m*-xylene at 120°. In one case the solid acetylide was treated with excess acetal and heated for three hours. In each instance some 2-ethoxy-3-nonyne was obtained, but the yields were quite low. No acetylenic ether could be identified among the reaction products when sodium acetylide was employed in the above media.

Discussion of Results

That the reaction studied in this investigation proceeds through replacement of one alkoxyl group of the acetal or ketal by the acetylenic radical was clearly demonstrated by synthesizing 1-phenyl-1-ethoxy-2-heptyne and 2-ethoxy-3-nonyne by two independent methods, involving the use of different intermediates. Such a mechanism accounts for the formation of identical products when the following reactions were carried out



Each reaction of dialkoxyalkane with hexynylmagnesium bromide was carried out under identical conditions of time, temperature and concentration of reactants, and a very marked variation in the reactivity of the different types of alkoxy compounds was noted. 1,2-Dimethoxyethane, given a longer reaction period, produced only 15% of acetylenic ether. Under the standard conditions, the acetals of formaldehyde yielded 31 to 35% of ether, acetaldehyde and propionaldehyde, 46 to 49%, 2-hexanone, 57%, *n*-butylpropiolaldehyde, 62% and benzaldehyde, 66%.

This method of acetylenic ether synthesis is a very general one, in so far as alkyl ethers of primary, secondary or tertiary acetylenic carbinols may be obtained, depending on whether acetals of formaldehyde, higher aldehydes or ketones are used as starting materials. In addition, the intermediates needed for the secondary and tertiary acetylenic ethers are obtainable directly from acetylene and the alkylacetylenes, thus obviating the use of haloethers or acetylenic carbinols as such.

Summary

Various acetals and ketals have been found to react with alkynylmagnesium bromides to yield ethers of primary, secondary and tertiary acetylenic carbinols and glycols. The latter two types of acetylenic ethers were synthesized from intermediates obtained from acetylene and alkylacetylenes.

Acetals of formaldehyde, higher alkyl aldehydes, ketones and benzaldehyde exhibited a definite increase in reactivity, in the order named, which is explainable electronically.

Sodium acetylides have been shown to react only to a slight extent with acetals in various solvents.

Several new acetylenic ethers have been reported.

A convenient method for the synthesis of 1,2-dimethoxyethane in good yields has been described.

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