

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

Acetylenic Alcohols from α,β -Unsaturated Aldehydes and Ketones¹BY G. F. HENNION AND D. J. LIEB²

Introduction

The addition of Grignard reagents to α,β -unsaturated carbonyl compounds has been studied extensively since Kohler's³ first observation of 1,4 addition in reactions of this type and the chemistry of the competing 1,2 and 1,4 reactions has received considerable attention.⁴ It appears that the mode of addition usually depends on the chemical character of the reactants, although certain metal salts may also influence the course of the reaction.⁵ Generally, however, if the carbonyl group is very reactive, 1,2 addition predominates. Thus α,β -unsaturated aldehydes add mainly in the 1,2 position, except with *t*-alkyl Grignard reagents, where considerable 1,4 addition may occur.⁶ Organo-zinc compounds usually resemble the magnesium compounds in this respect, but the more reactive organo-alkali compounds favor 1,2 addition.⁷

A recent new application of this type of reaction is the addition of sodium acetylide (in liquid ammonia) to certain α,β -unsaturated aldehydes, reported by Jones and McCombie,⁸ whereby 1,2 addition occurs, yielding ethynyl carbinols. This reaction has also been studied in this Laboratory and extended to include several α,β -unsaturated ketones.⁹ Because of the ionic character and notable reactivity of sodium acetylide in liquid ammonia, it was felt that this reagent would add to a variety of α,β -unsaturated carbonyl compounds in the 1,2 manner only, *i. e.*, by anion addition at the carbon atom of lowest electron density.¹⁰

(1) Paper XLVII on the chemistry of substituted acetylenes; previous paper, *THIS JOURNAL*, **65**, 1847 (1943).

(2) Present address, Casein Company of America, Bainbridge, N. Y.

(3) Kohler, *Am. Chem. J.*, **31**, 642 (1904).

(4) Gilman, "Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 506, 672, 1920.

(5) Kharasch and Tawney, *THIS JOURNAL*, **63**, 2308 (1941).

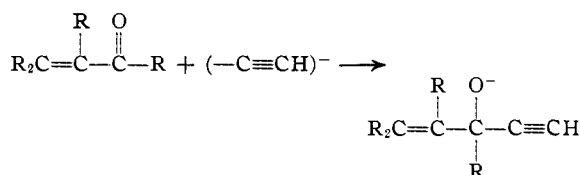
(6) Stevens, *ibid.*, **56**, 1425 (1934); **57**, 1112 (1935).

(7) Gilman and Kirby, *ibid.*, **63**, 2046 (1941).

(8) Jones and McCombie, *J. Chem. Soc.*, 733 (1942).

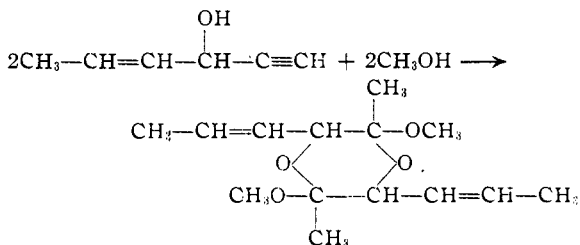
(9) Due to the unavoidable delay in the availability of foreign journals, the work of Jones and McCombie⁸ did not come to our attention until the present study had been concluded.

(10) A comparison of the reactions of HX, RMgX (and similar organometallic compounds) and NaC≡CH with the system $\begin{array}{c} \text{R} \\ | \\ \text{C}=\text{C} \\ | \\ \text{C}=\text{O} \end{array}$ suggests a simple explanation of the various modes of addition. Where the addendum molecule behaves as a cationoid donor (as would be the case with HX) the initial attack should be on the oxygen of $\text{C}=\text{O}$. Resonance may now operate to transfer the seat of minimum electron density to the β -ethylenic carbon where the subsequent union of the anionoid center makes for an over-all 1,4 addition. With anionoid reagents, however, the initial reaction should be one of direct union of the anionoid group to the carbon atom of lowest electron density, *i. e.*, the carbon of $\text{C}=\text{O}$, resulting in 1,2 addition. Since sodium acetylide in liquid ammonia is here an anionoid reagent, it should react by the latter mechanism unless steric repulsions force the anionoid addition on the β -ethylenic carbon.—G. F. H.



This was found to be the case in the reactions studied, namely, with crotonaldehyde, methyl vinyl ketone, ethylidene acetone, mesityl oxide, and benzalacetone. With cinnamaldehyde, however, a brown, amorphous, and apparently polymeric condensation product was obtained, from which no definite compound could be isolated. Though the purified enyne alcohols were obtained in rather low yield, they gave no test for the carbonyl group with 2,4-dinitrophenylhydrazine reagent.

When a sample of 4-hexen-1-yn-3-ol (from crotonaldehyde) was reacted with methanol in the presence of mercuric oxide and a little boron trifluoride, the usual mode of addition¹¹ took place, and 2,5-dimethoxy-2,5-dimethyl-1,3-dipropenyl-1,4-dioxane was formed.



The various compounds are described in Table I.

Experimental

The Reaction of Crotonaldehyde with Sodium Acetylide.—One hundred and seventy-five grams (2.5 moles) of freshly distilled crotonaldehyde, diluted with an equal volume of dry ether, was added dropwise (two hours) to 2.5 moles of sodium acetylide¹² in two liters of liquid ammonia. Mechanical stirring was used throughout the reaction and an outside temperature of about -60° maintained by cooling with solid carbon dioxide and acetone. Stirring was continued for three hours after the final addition of crotonaldehyde, the cooling bath removed, and the ammonia evaporated. The residue was covered with 500 ml. of ether, and 200 ml. of water added dropwise followed by careful acidification with cold 50% sulfuric acid. The ether layer was separated, and the aqueous solution extracted with two 100-ml. portions of ether. The combined ethereal extract was washed with saturated brine, dilute sodium carbonate solution, again with brine, and dried over anhydrous magnesium sulfate. A small amount of hydroquinone was added, the ether distilled off, and the product vacuum distilled rapidly to a receiver packed in ice and salt. Thirty-two grams of polymeric residue remained behind, corresponding to 13% of the theoretical

(11) Hennion and Murray, *THIS JOURNAL*, **64**, 1220 (1942).

(12) Hennion, *Proc. Ind. Acad. Sci.*, **47**, 116 (1938).

TABLE I
 PHYSICAL CONSTANTS AND ANALYTICAL DATA

Compound	Source	Yield, %	B. p., °C.		n_D^{20}	d_{20}^{20}
			°C.	Mm.		
4-Hexen-1-yn-3-ol ^a	Crotonaldehyde	46	66	20	1.4650	0.9155
3-Methyl-4-penten-1-yn-3-ol	Methyl vinyl ketone ^b	21	58-59	60	1.4444	.8895
3-Methyl-4-hexen-1-yn-3-ol	Ethylidene acetone ^c	27	61-62	25	1.4530	.8886
3,5-Dimethyl-4-hexen-1-yn-3-ol	Mesityl oxide	24	65-66	17	1.4629	.8939
3-Methyl-5-phenyl-4-penten-1-yn-3-ol	Benzalacetone	20	114-116	4	M. p.,	50-51
2,5-Dimethoxy-2,5-dimethyl-3,6-dipropenyl-1,4-dioxane		22	M. p.,			119-120

Formula	Mol. wt.		Carbon, %		Hydrogen, %		MR	
	Calcd.	obsd.	Calcd.	Obsd. ^d	Calcd.	Obsd. ^d	Calcd.	Obsd.
C ₆ H ₈ O							28.96	29.00
C ₈ H ₈ O	96	97	75.00	75.20	8.33	8.4	28.96	28.69
C ₇ H ₁₀ O	110	108	76.36	76.80	9.09	9.3	33.58	33.45
C ₈ H ₁₂ O	124	125	77.42	77.41	9.68	9.4	38.20	38.24
C ₁₂ H ₁₂ O	172	174	83.72	83.12	6.98	6.91		
C ₁₄ H ₂₄ O ₄ ^e	256	258	65.62	65.67	9.37	9.43		

^a Previously reported by Lespieau and Lombard, *Compt. rend.*, **198**, 2179 (1934), and by Jones and McCombie, ref. 8.
^b Supplied by the Jackson Laboratory, du Pont Company. ^c Prepared according to Grignard and Fluchaire, *Ann. chim.*, [10] **9**, 10 (1928). ^d Analyses (except last line) by Arlington Laboratories, Fairfax, Va. ^e Analysis for methoxyl, % calcd., 24.2; obsd., 23.8.

yield of carbinol. The distillate was put through a small Fenske-Whitmore column, yielding 112 g. of 4-hexen-1-yn-3-ol, a colorless liquid, b. p. 66° at 20 mm.

Other Reactions with Sodium Acetylide.—The above procedure was used. One and four-tenths moles of methyl vinyl ketone yielded 30 g. of the carbinol and 5 g. of residue. Two moles of ethylidene acetone gave the expected carbinol and 26 g. of residue, most of which could be distilled with decomposition at 65-127° at 4 mm. Mesityl oxide (3 moles) returned 132 g. unreacted, 44 g. of the carbinol, and 29 g. of higher boiling residue. One mole of benzalacetone gave only 35 g. of carbinol and 83 g. of higher boiling material. One and one-half moles (198 g.) of cinnamaldehyde formed 211 g. of brown amorphous solid, soluble in benzene and ligroin.

Addition of Methanol to 4-Hexen-1-yn-3-ol.—The previously described procedure¹¹ with 96 g. of 4-hexen-1-yn-3-ol

gave 28 g. of solid after distillation of the excess methanol. Several crystallizations from aqueous methanol afforded a white crystalline solid, m. p. 119-120°.

Summary

1. The 1,2 addition of sodium acetylide to a number of α,β -unsaturated carbonyl compounds is reported and five products are described.
2. The addition of methanol to 4-hexen-1-yn-3-ol gave a cyclic addition product identified as 2,5-dimethoxy-2,5-dimethyl-3,6-dipropenyl-1,4-dioxane.

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The Synthesis of *l*-Roemerine¹

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Roemerine was discovered in the papaveraceous plant *Roemeria refracta*, D.C., by Konowalowa, Yunussov and Orekhov² who assigned to it the formula C₁₈H₁₇O₂N. Subsequently, with the aid of degradative experiments, they demonstrated that roemerine is a methylenedioxy-aporphine,³ possessing the structure VII. This alkaloid being the first example of a naturally occurring aporphine carrying no substituents except in the tetrahydroisoquinoline moiety, it was of interest to attempt its synthesis which, furthermore, was desirable to confirm the proof of the structure VII assigned to it.

For this synthesis it was necessary to prepare β -3,4-methylenedioxy-phenylethylamine and 2-

nitrophenylacetic acid required as starting materials.

From the amine I and the acid chloride II, 6'-nitrophenylaceto- β -3,4-methylenedioxy-phenylethyl amide III was obtained which, by a modified Bischler-Napieralsky reaction, was converted to 6'-nitro-1-benzyl-6,7-methylenedioxy-3,4-dihydroisoquinoline IV. The methiodide V of this base was reduced with zinc and hydrochloric acid to 6'-amino-1-benzyl-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline VI isolated as the dihydrochloride. In the Pschorr ring-closure reaction this dihydrochloride gave rise to *dl*-roemerine VII and an unidentified by-product. The racemic base was resolved into its optical isomers by treatment first with *d*-tartaric acid and then with *l*-tartaric acid. Synthetic *l*-roemerine was found to exhibit dimorphism. For

(1) Published as N. R. C. No. 1184.

(2) Konowalowa, Yunussov and Orekhov, *Bull. soc. chim.*, [5] **6**, 811 (1939).

(3) *Ibid.*, [5] **6**, 1479 (1939); [5] **7**, 70 (1940).