

nickel⁶ as the catalyst. In each experiment after 0.1 mole of the azo compound, 0.25 mole of the aldehyde and 2.0 g. of sodium acetate had been dissolved in 150 cc. of alcohol, from 2.0 g. to 40 g. of Raney nickel was added and the mixture placed in the machine at an initial pressure of 45 lb. It was found that 10 g. of Raney nickel was best, since it was the smallest quantity which gave a smooth and rapid reduction. The mixture was shaken until no more hydrogen was absorbed, usually from one to two hours, 0.3–0.4 mole of hydrogen being taken up. After the catalyst had been removed by filtration, the solvent was distilled on the steam bath. In the case of the lower molecular weight amines the reaction mixture was acidified before the evaporation of the solvent. The residue, made basic if necessary, was extracted with ether and the ether dried over sodium hydroxide. After the removal of the drying agent, the ether was evaporated and the products obtained by distillation, usually at reduced pressure.

Amines from Azobenzene.—Using the general procedure described above *N,n*-butylaniline was obtained from azobenzene in 71% yield and identified as the *p*-bromobenzenesulfonamide, m. p. 85–86° (87°).⁷ Similarly *N-n*-heptylaniline was obtained in 74% yield and also identified as the *p*-bromobenzenesulfonamide, m. p. 114–115° (115°).⁸

N-Benzylaniline was isolated in 49% yield as the hydrochloride, m. p. 210–212° (214–216°).⁸

N,N-Dimethyl-*N',N'*-di-*n*-butyl-*p*-phenylenediamine, prepared similarly from *N,N*-dimethyl-*p*-aminoazobenzene and *n*-butyraldehyde in 76% yield, b. p.

(6) Covert and Adkins, *THIS JOURNAL*, **54**, 4116 (1932).

(7) Marvel and Smith, *ibid.*, **45**, 2696 (1923).

(8) Brand, *Ber.*, **42**, 3460 (1909).

150–175° (20 mm.), was identified as the picrate, m. p. 121–122°.

Anal. Calcd. for C₂₂H₃₁O₇N₅: N, 14.7. Found: N, 14.8.

A 73% yield of *n*-butylaniline was also obtained in this reaction.

N,N-Di-*n*-butyl-*p*-aminophenol was obtained in the same way from *p*-hydroxyazobenzene and *n*-butyraldehyde. It was isolated as the benzoate by treatment with benzoyl chloride and aqueous alkali; yield 46%. This benzoate melted at 232–233° after two crystallizations from acetic acid.

Anal. Calcd. for C₂₁H₂₇O₂N: N, 4.31. Found: N, 4.47.

1-(*N,N*-Di-*n*-butylamino)-2-naphthol was prepared in 41% yield from 1-phenyl-azo-2-naphthol and *n*-butyraldehyde. It was isolated by adding water to the reaction mixture after half of the alcohol had been distilled, m. p. 106–107°. As it darkened rapidly on standing, it was stored as the hydrochloride, m. p. 225–227°.

Anal. Calcd. for C₁₈H₂₆ONCl: Cl, 11.6. Found: Cl, 11.5.

Summary

Three alkyylanilines have been prepared in 49–74% yield by treating an alcoholic solution of azobenzene and an aldehyde with hydrogen in the presence of Raney nickel and sodium acetate. When an activating group such as hydroxyl or dimethylamino is present in the *ortho* or *para* position, a tertiary amine is produced.

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The Synthesis of Certain Unsaturated Substances from β -Ionone and Substituted Vinylacetylenes

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Substances prepared by condensation of β -ionone so that the β -ionone ring is retained, and a longer unsaturated side chain results, are of interest for at least two reasons. First, there is the possibility that such substances may exhibit the physiological activity of Vitamin A, at least in some degree. Second, the physiological properties of such synthetic substances shed light on the specific structural arrangement necessary for a molecule to possess Vitamin A activity.

It was decided to investigate the condensation products of vinylacetylene, and two of its simple

derivatives, with β -ionone. The condensation product from β -ionone and vinylacetylene itself has already been prepared by Zal'kind, Zonis and Blokhin² who reported that their product was physiologically inactive. However, the unsaturated carbinol derived from this condensation product by partial reduction of the triple bond has never been reported. And there is no published description of any condensation products of β -ionone with derivatives of vinylacetylene.

The series of transformations performed in the present investigation is illustrated by formulas I–VII inclusive. It was hoped at the outset that

(1) Part of the material of this paper is abstracted from a thesis submitted to the Massachusetts Institute of Technology by Ida Rovno in partial fulfillment of the requirements for the degree of Bachelor of Science.

(2) Zal'kind, Zonis and Blokhin, *Compt. rend. acad. sci., U. S. S. R.*, **2**, 57 (1935).

Vitamin A activity. None of them proved to be physiologically potent, but it is still impossible to decide whether the carbinols (VIII) are active and the work is being continued.

In order to have available compounds of known structure for reference compounds, the series of carbinols (V), (VI), and (VII) were prepared, no novel methods being required for their preparation.

Experimental

The β -ionone and the vinylacetylene used in this work were very kindly furnished by the du Pont Company.

Tetrahydroionone was prepared by complete hydrogenation of the β -ionone, using Adams catalyst.

2-Methyl-butene-1-yne-3 was prepared by dehydration of dimethylethynylcarbinol, prepared according to Froning and Hennion.⁵

Into 60 g. (0.588 mole) of acetic anhydride containing 1 cc. of sulfuric acid was dropped 60 g. (0.715 mole) of dimethylethynylcarbinol. The apparatus was swept with nitrogen and the temperature and rate of addition were maintained so as to keep the temperature of the distillate below 50°. The distillate was carefully fractionated. Twenty-three grams of hydrocarbon was obtained, b. p. 35–40°, yield 50%.

3-Methyl-pentyne-1-ene-3 was obtained in a similar manner from methylethylethynylcarbinol, prepared according to Campbell, Campbell and Eby.⁶ A 55% yield of the hydrocarbon was obtained, b. p. 70–72°.

Addition of Vinylacetylene Derivatives to β -Ionone.—General procedures for the addition reactions were developed as follows. When potassium *t*-amylate was used as condensing agent, the vinylacetylene derivative was dropped into the equivalent amount of potassium *t*-amylate dissolved in *t*-amyl alcohol. The temperature of the solution was then brought to –10° and maintained at this point throughout the reaction. An equivalent amount of β -ionone was dropped slowly into the cold solution, and the whole was stirred in a nitrogen atmosphere for seven hours, then worked up in the usual manner. The yield of acetylenic carbinol obtained in this way was only 11–20%, depending on the vinylacetylene derivative used, and most of the ionone was resinified.

The vinylacetylenic Grignard reagents were more satisfactory, furnishing the carbinols IIa, IIb, and IIc, in yields of 59%, 48%, and 52%, respectively, based on the amount of β -ionone used. The reaction was carried out as follows. The vinylacetylene derivative (0.150 mole) was dropped into an equivalent amount of ethylmagnesium bromide solution. The rate of addition was determined by the refluxing of the ether. The solution was heated for one hour after spontaneous refluxing had ceased. The β -ionone (0.125 mole) was then slowly dropped in, after which the reaction mixture was refluxed for six hours. The condensation product was isolated and purified by vacuum distillation. In every case the condensation product was analyzed by quantitative catalytic hydrogenation to determine the number of double bonds,

and the hydroxyl content was determined in the Grignard machine,⁷ as a measure of the relative amounts of 1,2 and 1,4 addition. These data were used to compute the amount of carbinol present in the addition product, and the yields given above were based on these analytical results. These and other data relative to the carbinols are included in Table I.

Partial Reduction of the Acetylenic Carbinols II.—The procedure for the reductions was identical in every case. The acetylenic carbinol was dissolved in absolute alcohol, a palladium–calcium carbonate catalyst⁸ was added, and the substance was shaken with hydrogen, measured from a 1000 cc. buret, until the theoretical amount of gas was absorbed. The catalyst was filtered off and the ethylenic carbinol distilled, after evaporation of the alcohol. In this way the three ethylenic carbinols IIIa, IIIb, and IIIc were prepared in nearly quantitative yield. The unsaturation of the carbinols was checked by quantitative catalytic hydrogenation. The data relative to these carbinols are included in Table I.

Addition of Vinylacetylene Derivatives to Tetrahydroionone.—The condensation of vinylacetylene derivatives with tetrahydroionone proceeded smoothly using both sets of conditions described above for β -ionone. Potassium *t*-amylate was preferred as condensing agent since at 10–20° the reaction proceeded smoothly to completion in two hours (note higher temperature than could be used with β -ionone). It was necessary to reflux the vinylacetylenic Grignard reagents for eighteen hours to obtain complete condensation with tetrahydroionone. Both methods furnished the acetylenic carbinols V in 80% yields.

As usual, quantitative catalytic hydrogenation was used to determine the number of double bonds in the products. The data are included in Table I.

The partial reduction of the acetylenic carbinols V to the corresponding olefins VI was accomplished exactly as previously described for compounds II. The data for the carbinols VI are included in Table I.

The saturated carbinols VII were prepared by complete saturation, using Adams catalyst, of the carbinols of the structures II and V, for comparison of their physical properties. The properties of the carbinols VII from both series are included in Table I.

Rearrangement of the Unsaturated Carbinols (III) and (VI).—Attempts were made to cause the 1,5 shift similar to an "allyl" rearrangement to proceed by boiling with acetic anhydride containing mineral acid, by heating with trichloroacetic acid, and by treating the corresponding bromides, as obtained from the carbinols with phosphorus tribromide, with sodium acetate in various solvents. These attempts have so far been unsuccessful but the project has not been abandoned.

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(5) Froning and Hennion, *THIS JOURNAL*, **62**, 654 (1940).

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

(7) (a) Kohler, Stone and Fuson, *ibid.*, **49**, 3181 (1927). (b) Kohler and Richtmyer, *ibid.*, **52**, 3736 (1930).

(8) Busch and Stöve, *Ber.*, **49**, 1064 (1916).

TABLE I

	B. p., °C. (2 mm.)	n_D^{25}	No. double bonds ^a	Formula	Analyses, %				
					Carbon		Hydrogen		
					Calcd.	Found	Calcd.	Found	
R = 2,2,6-trimethylcyclohexenyl- Δ^6									
Vinylacetylenic Carbinols II Derived from β -Ionone									
IIa	5-Hydroxy-5-methyl-7-(R)-heptadiene-1,6-yne-3 ^g	155-160	1.5437 ^b	4.77	C ₁₇ H ₂₄ O	83.6	83.4	9.85	10.6
						83.6			10.4
IIb	5-Hydroxy-2,5-dimethyl-7-(R)-heptadiene-1,6-yne-3 ^h	165-170	1.5395 ^b	5.00	C ₁₈ H ₂₆ O	83.7	83.4	10.1	10.2
						83.5			10.2
IIc	6-Hydroxy-3,6-dimethyl-8-(R)-octadiene-2,7-yne-4 ⁱ	170-175	1.5387 ^b	4.77	C ₁₉ H ₂₈ O	83.8	83.5	10.3	10.5
						83.7			10.7
Partially Reduced Carbinols III Derived from Carbinols II									
IIIa	5-Hydroxy-5-methyl-7-(R)-heptatriene-1,3,6 ^d	155-160	1.5137 ^b	3.83					
IIIb	5-Hydroxy-2,5-dimethyl-7-(R)-heptatriene-1,3,6 ^e	165-170	1.5147 ^b	3.80					
IIIc	6-Hydroxy-3,6-dimethyl-8-(R)-octatriene-2,4,7 ^f	170-175	1.5137 ^b	3.79					
R = 2,2,6-trimethylcyclohexyl									
Vinylacetylenic Carbinols V Derived from Tetrahydroionone									
Va	5-Hydroxy-5-methyl-7-(R)-heptene-1-yne-3	155-160	1.4982	3.26	C ₁₇ H ₂₆ O	82.2	82.4	11.3	11.9
						81.9			12.1
Vb	5-Hydroxy-2,5-dimethyl-7-(R)-heptene-1-yne-3	165-170	1.4970	2.88	C ₁₈ H ₃₀ O	82.4	82.7	11.4	11.5
						82.2			11.7
Vc	6-Hydroxy-3,6-dimethyl-8-(R)-octene-2-yne-4	170-175	1.4945	3.19	C ₁₉ H ₃₂ O	82.6	82.1	11.6	12.1
						82.2			12.0
Partially Reduced Carbinols VI Derived from Carbinols V									
VIa	5-Hydroxy-5-methyl-7-(R)-heptadiene-1,3	150-155	1.4848	2.03					
VIb	5-Hydroxy-2,5-dimethyl-7-(R)-heptadiene-1,3	160-165	1.4834	1.91					
VIc	6-Hydroxy-3,6-dimethyl-8-(R)-octadiene-2,4	165-170	1.4815	1.89					
Completely Saturated Carbinols VII									
VIIa	5-Hydroxy-5-methyl-7-(R)-heptane	145-150	1.4756 (from IIa) ^c		C ₁₇ H ₃₄ O	80.3	80.6	13.4	13.9
			1.4752 (from Va) ^c			80.2			13.5
VIIb	5-Hydroxy-2,5-dimethyl-7-(R)-heptane	155-160	1.4740 (from IIb) ^c		C ₁₈ H ₃₆ O	80.6	80.7	13.5	13.8
			1.4749 (from Vb) ^c			80.4			13.4
VIIc	6-Hydroxy-3,6-dimethyl-8-(R)-octane	160-165	1.4740 (from IIc) ^c						
			1.4744 (from Vc) ^c						

^a Determined by catalytic addition of hydrogen. ^b n_D^{25} . ^c n_D^{25} . ^d Prepared from IIa. ^e Prepared from IIb. ^f Prepared from IIc. ^g In the Grignard machine 0.176 g. yielded 16.5 cc. methane; calcd. 18 cc. This corresponds to 91% 1,2 addition product. ^h In the Grignard machine 0.147 g. yielded 12.8 cc. of methane; calcd. 14.2 cc. This corresponds to 90% 1,2 addition product. ⁱ In the Grignard machine 0.197 g. yielded 17.0 cc. of methane; calcd. 18 cc. This corresponds to 94% 1,2 addition product.

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Summary

A number of unsaturated carbinols have been prepared by interaction of vinylacetylene and its

derivatives with β -ionone and tetrahydroionone. The vinylacetylene derivatives were prepared in improved yields by dehydration of the corresponding acetylenic carbinols with acetic anhydride. The β -ionone derivatives were tested for Vitamin A activity but none of them showed any such activity.

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