was heated in an oil-bath at 130–135° for a varying time. The mixture was then steam distilled, charcoaled and acidified to Congo red paper with concentrated hydrochloric acid. From this the condensation product was isolated and purified.

2-Arsono-4-nitrophenylglycine formed by such a condensation was reduced by means of molecular hydrogen in the presence of nickel[6] to the corresponding amine.

Summary

1. 2-Chloro-5-carboxyphenylarsonic acid was condensed with ethanolamine, phenol and glycine.
2. Under the conditions of an Ullmann reaction, 2-chloro-5-cyanophenylarsonic acid reacted with phenol.
3. 2-Chloro-5-nitrophenylarsonic acid was successfully condensed with glycine, and the corresponding amino derivative of the condensation product synthesized.
4. Under the ordinary conditions found successful for condensing halogenophenylarsonic acids 2-chloro-5-aminophenylarsonic acid did not condense with itself, isoamylamine, ethanolamine or *p*-chlorophenol, and its acetyl derivative did not react with aniline or *p*-chlorophenol.
5. All attempted condensations between 2-chloro-5-hydroxyphenylarsonic acid and itself, ethanolamine or *p*-chlorophenol, and between its carbethoxy derivative and aniline or *n*-butyl amine were unsuccessful.
6. Apparently, the presence of an amino or a hydroxyl grouping, in the para position to an activated chlorine, strengthens the attachment of the halogen to carbon, and makes it less labile.
7. Several organic arsenicals, incidental to the problem, have been prepared and identified for the first time.

LINCOLN, NEBRASKA RECEIVED JANUARY 16, 1935

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(6) Stevinson, Doctor's Thesis, University of Nebraska, 1934.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 117]

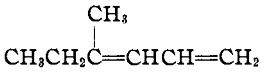
Synthetic Studies with the Ionones. I. Synthesis of an Alcohol Related to Vitamin A

BY NICHOLAS A. MILAS AND AMBROSE MCALEVY[1]

A considerable amount of research has been done during the past few years in the field of vitamin A and related naturally occurring products. This work culminated in the important studies of Karrer and his students[2] in the determination of the structure of this vitamin. The vitamin itself has not yet been synthesized, nor have any of its derivatives or other substances closely related to it.

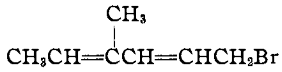
A little over two years ago, we began working in this field with the object of procuring some necessary information prior to making attempts to synthesize the vitamin itself or some one of its derivatives. Since much work is being done at present in this field by other investigators, it seems advisable to publish some of our preliminary results although the work has not yet been completed.

When 1-bromo-4-methyl-2,4-hexadiene (II) is condensed by means of the Grignard reaction with α-ionone,[3] 1,2 addition takes place yielding, after hydrolysis, the tertiary alcohol (III). That the Grignard reaction results in 1,2 addition in the case of α-ionone has also been shown by Karrer and his students[4] using allylmagnesium bromide.



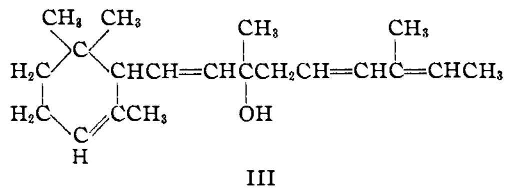
$CH_3CH_2\overset{CH_3}{\overset{|}{C}}=CHCH=CH_2$

I

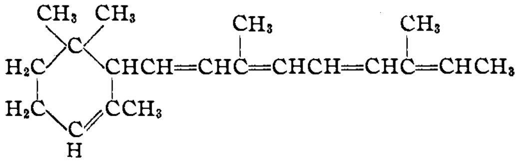


$CH_3CH=\overset{CH_3}{\overset{|}{C}}CH=CHCH_2Br$

II



III



IV

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(1) Abstracted from Part II of the Ph.D. Dissertation of Ambrose McAlevy, M. I. T., June, 1934.

(2) Karrer, Morf and Schopp, *Helv. Chim. Acta*, **14**, 1431 (1931); **16**, 557 (1933).

(3) The condensation with β-ionone is being investigated.

(4) Karrer, Salomon, Morf and Walker, *Helv. Chim. Acta*, **15**, 878 (1932).

Neither the methylhexadiene bromide nor the methylhexadiene (I) from which this bromide was prepared were known previously. Their synthesis had to be accomplished and their structure definitely settled prior to the final condensation.

The tertiary alcohol (III) is a highly viscous liquid of light greenish-yellow or olive color; it is very sensitive to auto-oxidation, and heat, even under very low pressures, decomposes it into a red substance. When it is dehydrated with phenyl isocyanate or potassium hydrogen sulfate, water splits out and a highly colored hydrocarbon, probably the polyene (IV) or some cyclic form of this, is obtained. This hydrocarbon has properties that resemble those of carotene and vitamin A. For example, it absorbs oxygen and bromine with great rapidity, and yields instantly with antimony trichloride, in chloroform solution, a purple color turning immediately to blue. The structure of this hydrocarbon has not yet been established with absolute certainty.

Experimental Part

Methylethylallylcarbinol.—This carbinol was first prepared by Saytzeff[5] in 17% yield by condensing methyl ethyl ketone with allyl iodide in the presence of zinc. In the present work, this alcohol was prepared by the Grignard reaction using either allyl chloride or allyl bromide; a yield of 50–60% was obtained from the chloride and about 42% from the bromide. In a typical experiment 62.5 g. of magnesium was activated by the method of Gilman,[6] and to this was added 10 g. of allyl chloride[7] in 10 cc. of anhydrous ether. As soon as the Grignard reagent began to form vigorously, 200 cc. of anhydrous ether was added, then a mixture of 400 cc. of ether containing 156 g. of pure methyl ethyl ketone and 190 g. of allyl chloride was added drop by drop, the rate of addition being such as to keep the reaction proceeding with sufficient vigor to cause the ether to reflux at a rate of about one drop per second. At the end of six hours, the mixture was poured into crushed ice containing 6 *N* sulfuric acid, and the ether layer removed and dried over anhydrous sodium sulfate. This mixture yielded 154 g. (52%) of methylethylallylcarbinol boiling at 69–71° (60 mm.), and 138–139° (atm. press.) with slight decomposition. Saytzeff gives 139° as its b. p. The carbinol is a colorless, slightly viscous liquid of camphoraceous odor, having the following physical constants: d^{25}_{4} 0.83653; n^{25}_{D} 1.4309; M_R, calcd. for $C_7H_{14}O$, 35.34; found, 35.39.

4-Bromo-4-methyl-1-hexene.—This methylhexene bromide was prepared by carefully and slowly dropping 20 g. of methylethylallylcarbinol into a flask immersed in ice and containing 18 g. of phosphorus tribromide. The flask with its contents was then heated gently with warm water for a few minutes and the mixture separated from the phosphorous acid and fractionated under reduced pressure. A colorless liquid (15 g.), which became golden-yellow on exposure to air, distilled at 59.8° (27 mm.), d^{25}_{4} 1.1162.

Anal. Calcd. for $C_7H_{13}Br$: Br, 45.14. Found: Br, 45.22, 44.89.

4-Methyl-1,3-hexadiene.—This hexadiene has been prepared by the dehydration of methylethylallylcarbinol or by the elimination of hydrogen bromide from 4-bromo-4-methyl-1-hexene.

(1) **From the Carbinol.**—Phthalic and acetic anhydrides, formic and oxalic acids and potassium hydrogen sulfate were used to dehydrate this carbinol, but the last one gave the best results. Ten grams of methylethylallylcarbinol was mixed with 5 g. of potassium hydrogen sulfate and the mixture was slowly distilled in a flask provided with a small fractionating column. The distillate came over in two layers, the bottom of which was water and was therefore discarded, while the hydrocarbon layer was redistilled and the product boiling below 100° collected and dried over calcium chloride; yield, 7.5 g. or 88.3%. This was fractionated and the largest portion boiling at 97–98° collected and analyzed. It shows the constants: d^{25}_{4} 0.7324; n^{25}_{D} 1.4342; M_R, calcd. for C_7H_{12}, 33.463, found, 34.135; exaltation, 0.672.

Anal. Calcd. for C_7H_{12}: C, 87.42; H, 12.59. Found (micro-method): C, 86.81; H, 12.46.

When titrated at low temperatures by the bromide–bromate method, it was found to absorb bromine equivalent to 2.08 and 1.93 double bonds; calcd. 2.00. That the double bonds in this diene are conjugated is shown by the exaltation and by the fact that it combines with maleic anhydride in benzene solution to form a white crystalline substance melting at about 170°. The diene itself is a colorless liquid of characteristic odor. Upon standing in the air, it auto-oxidizes, forming a peroxide, and polymerizes at the same time. It can be distilled from metallic sodium but with some loss due to polymerization.

(2) **From 4-Bromo-4-methyl-1-hexene.**—The same methylhexadiene can be prepared in a yield of 78% from 4-bromo-4-methyl-1-hexene by distilling the latter with solid potassium hydroxide. When a mixture of 6 g. of bromomethylhexene and 10 g. of solid potassium hydroxide is slowly distilled, a product is formed which, when redistilled over anhydrous aluminum oxide, yields 2.54 g. of pure methylhexadiene having the same properties as that obtained by the dehydration of methylethylallylcarbinol.

(3) **Proof of the Structure of Methylhexadiene.**—That the methylhexadiene reported in the present work has the structure (I) was shown by oxidation experiments. Since ozonization failed to yield conclusive results, the diene was oxidized in the cold with alkaline potassium permanganate. To 0.41 g. of methylhexadiene was added slowly 200 cc. of a 3% solution of potassium permanganate containing 4.5 g. of potassium carbonate. After two days of standing at room temperature, this mixture yielded 0.4479 g. of calcium oxalate which is equivalent to 72% yield of oxalic acid on the basis of structure (I). Since no other structure of methylhexadiene with a conjugated system of double bonds will yield oxalic acid as one of the oxidation prod-

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(5) Saytzeff, *J. Russ. Phys.-Chem. Soc.*, **24**, 469 (1892).

(6) Gilman, paper presented before "The Fourth Organic Chemistry Symposium," New Haven, Conn., December, 1931.

(7) This chloride was prepared in excellent yields by the method of Breckpot [*Bull. soc. chim. Belg.*, **39**, 464 (1930)].

ucts, it is concluded that our methylhexadiene has the structure (I).

As confirmatory evidence our methylhexadiene was oxidized with chromic acid in the presence of phosphoric acid in accordance with the method of Kuhn and L'Orsa,[8] and the amount of acetic acid formed determined quantitatively. Two experiments yielded the following results: acetic acid formed/mole of methylhexadiene, 1.15, 1.34; calcd. for structure (I), 1.05–1.45.

1,4-Dibromo-4-methyl-2-hexene.—To 2.2466 g. of 4-methyl-1,3-hexadiene in 50 cc. of anhydrous ether was very slowly and cautiously added at 0° 8.7 cc. of carbon tetrachloride solution of bromine containing 0.4283 g. of bromine per cc. Rapid addition of the bromine solution should be avoided since it results in the evolution of hydrogen bromide. After all of the bromine solution had been added, the mixture was allowed to stand at 0° over anhydrous calcium chloride for three hours, then removed, fractionated and the fraction boiling at 64–66° (4 mm.) collected and analyzed. This showed the following constants: d^{25}_4 1.5406; n^{25}_D 1.5206; MR, calcd. for $C_7H_{12}Br_2$ 49.75, found 50.56.

Anal. Calcd. for $C_7H_{12}Br_2$: Br, 62.47. Found: Br, 62.90, 62.94.

This dibromide is rather unstable and loses slowly, on standing at room temperature, hydrogen bromide. It is for this reason that the values obtained for the presence of one double bond by the bromide–bromate method are distinctly higher than the theoretical, being 1.33 and 1.21 instead of 1.00. It is further possible that this dibromide is contaminated with small amounts of the 1,2 addition product although Prévost[9] has already shown that addition of one mole of bromine to dienes of structure analogous to our methylhexadiene yielded chiefly the 1,4 addition product.

1,2,4-Tribromo-4-methylhexane.—In the preparation of this product, it was found nearly impossible to prevent the evolution of hydrogen bromide. The best results were given by the following procedure: to 6 g. of 4-bromo-4-methyl-1-hexene in 10 cc. of carbon tetrachloride, was slowly added, at the temperature of an ice-salt mixture, 13 cc. of carbon tetrachloride–bromine solution containing 5.6 g. of bromine. During the addition of bromine small pieces of solid carbon dioxide were dropped into the mixture to reduce the evolution of hydrogen bromide to a minimum. At the end of the reaction, the temperature of the mixture was allowed to rise to room temperature and the excess bromine and the solvent removed at low pressures leaving a yellowish oil. This was redissolved in anhydrous ether, the solution shaken with calcium chloride and the ether removed under reduced pressure, yielding a clear, slightly yellow product. Attempts to distil this, even at very low pressures, resulted in considerable decomposition. Its bromine content was found to be slightly lower than the theoretical, but it is known that bromides of this type fail to give good analyses.

Anal. Calcd. for $C_7H_{13}Br_3$: Br, 71.19. Found: Br, 68.91, 68.89.

Attempts to prepare 1-bromo-4-methyl-2,4-hexadiene by the elimination of two moles of hydrogen bromide from the above tribromide were not successful, so our attention was turned to 1,4-dibromo-4-methyl-2-hexene.

1-Bromo-4-methyl-2,4-hexadiene (II).—The success of the preparation of this compound depended entirely upon the fact that the bromine atom attached to the tertiary carbon atom 4 in 1,4-dibromo-4-methyl-2-hexene is more easily eliminated than the one attached to the primary carbon atom. It was hoped that elimination of hydrogen bromide would take place in such a way as to produce the desired diene. Of the various methods tried to cause this elimination, the one used by Willstätter and Bruce[10] was found to give the best results. A mixture of 1,4-dibromo-4-methyl-2-hexene and 3.0 g. of powdered potassium hydroxide was heated at 70° for one hour and the resulting product fractionated under reduced pressure, the fraction distilling at 90–95° (22 mm.) collected and analyzed. This showed the following constants: d^{25}_4 1.3226; n^{25}_D 1.5172; MR, calcd. for $C_7H_{11}Br$, 41.2, found 40.0. This bromide was prepared and purified several times, and complete elimination of small amounts of the dibromide was found to be extremely difficult without destroying the monobromide itself which is very unstable and difficult to handle.

Anal. Calcd. for $C_7H_{11}Br$: Br, 45.69. Found: Br, 46.28, 46.94.

This bromide is very unstable and in presence of oxygen undergoes both oxidation and polymerization. It reacts rather vigorously with maleic anhydride with considerable evolution of heat. The product formed was not investigated further.

3,7-Dimethyl-1-(1′,1′,3′-trimethyl-3′-cyclohexenyl-2′)-nona-1,5,7-trien-3-ol (III).—A mixture of 3 g. of 1-bromo-4-methyl-3,4-hexadiene and 3.5 g. of α-ionone[11] in 100 cc. of anhydrous ether was dropped slowly into 0.5 g. of magnesium activated as described on page 581. The reaction proceeded so vigorously that the ether refluxed rather rapidly. As soon as the reaction subsided, the reaction flask was stoppered and allowed to stand at 0° for four days. The mixture was then hydrolyzed in the usual manner, the ether layer containing the carbinol separated, and dried over anhydrous sodium sulfate. An attempt was made at this stage to extract the carbinol from the ether solution by means of finely powdered anhydrous calcium chloride. This method of isolation of the carbinol was unsuccessful. The ether was therefore removed from the reaction products and the residue fractionated under reduced pressure. All of the unconverted α-ionone and other more volatile products came over below 71° (0.5 mm.), and since decomposition began to set in, the distillation was discontinued. An attempt was then made to crystallize the non-volatile sirupy material from a 1:1 mixture of methyl alcohol and petroleum ether. When this mixture was cooled in an ice–salt bath, a greenish-yellow but amorphous solid precipitated out, which melted into an oil slightly below room temperature. Several attempts made to crystallize this substance yielded exactly the same results. The precipitate was finally

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[8] Kuhn and L'Orsa, *Z. angew. Chem.*, **44**, 853 (1931).

[9] Prévost, *Bull. soc. chim.*, **43**, 996 (1928).

[10] Willstätter and Bruce, *Ber.*, **40**, 3994 (1907).

[11] α-Ionone was separated from a commercial preparation of ionones by the method of Chuit [Parry, "Essential Oils and Artificial Perfumes," Vol. II, page 218 (1932)] and was fractionated under reduced pressure and the fraction boiling at 128–129° (12 mm.) collected and used in these experiments.

removed, suspended in methyl alcohol in which it is nearly insoluble, the resulting mixture centrifuged and the semi-solid separated out and subjected to a high vacuum in order to remove traces of the solvent.

Anal. Calcd. for $C_{20}H_{32}O$: C, 83.25; H, 11.18. Found: C, 83.47; H, 11.07.

This carbinol is highly unsaturated and is very susceptible to air oxidation. It cannot be distilled without decomposition. When distilled with phenyl isocyanate, a nearly colorless hydrocarbon comes over which becomes immediately deep red upon condensation, and on redistillation comes over at about 101° (0.5 mm.). This highly colored hydrocarbon, which is also formed together with water by the distillation of the carbinol with potassium hydrogen sulfate, shows properties that resemble those of carotene and vitamin A. With a solution of antimony trichloride in chloroform, this hydrocarbon yields instantly a purple color which changes immediately into blue and finally on longer standing into light brown. On standing at room temperature in presence of air, it undergoes a change from a clear red to a dirty brown color. It decolorizes bromine water instantly, thereby changing into a light brown colored liquid. Unfortunately, the quantities obtained were too small to carry out further studies on the structure of this hydrocarbon. However, from its preparation and qualitative reactions, one may tentatively assign to it structure (IV), although cyclization might have occurred to produce a different structure. No definite answer with regard to the structure of this hydrocarbon can therefore be given at present.

Summary

1. The following compounds have been synthesized and some of their reactions studied: methylethylallylcarbinol, 4-methyl-1,3-hexadiene, 4-bromo-4-methyl-1-hexene, 1,4-dibromo-4-methyl-2-hexene, 1,2,4-tribromo-4-methylhexane and 1-bromo-4-methyl-2,4-hexadiene.

2. A carbinol, 3,7-dimethyl-1-(1′,1′,3′-trimethyl-3′-cyclohexenyl-2′)-nona-1,5,7-trien-3-ol, related to vitamin A has been synthesized by the condensation of 1-bromo-4-methyl-2,4-hexadiene with α-ionone in presence of magnesium. This carbinol yields on dehydration a highly colored hydrocarbon which has properties that resemble those of carotene and vitamin A.

CAMBRIDGE, MASS. RECEIVED JANUARY 17, 1935

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ILLINOIS]

The Structure of Troeger's Base

BY M. A. SPIELMAN[1]

Troeger's base $C_{17}H_{18}N_2$ is a substance formed by the condensation of formaldehyde with *p*-toluidine in acid solution.[2] Troeger assigned to his compound formula I and adduced as evidence two principal reactions. The first of these was with acetic anhydride to form a rather intractable diacetyl derivative which he believed to be dimolecular with respect to the base. The second reaction was with oxides of nitrogen and resulted in the evolution of carbon dioxide and the formation of a dinitrosamine of anomalous composition. Löb,[3] Goecke[4] and Lepetit, Maffei and Maimeri[5] have isolated Troeger's base, and the first two authors have proposed structures not in keeping with the empirical formula which now seems well established. Eisner and Wagner[6] have recently encountered the base in connection with their study of the condensation of aromatic amines with formaldehyde; they have confirmed earlier work in a general way and have suggested II as a tentative formula. Although this rationalizes the formation of a dinitroso and diacetyl derivative, it is obviously open to serious objections on stereochemical grounds.

Experiments described in this paper have led to an entirely different interpretation of the reactions of Troeger's base, and formula III is here offered as best representing the chemical properties of this interesting substance. The formula is drawn so that the tetrahydroquinazoline structure is apparent, but when a molecule is constructed from atomic models it is found to be symmetrical and composed of four six-membered rings condensed without strain.

The absence of any reaction with phenyl isocyanate or with phenyl mustard oil rendered improbable the presence of imino hydrogen atoms, and resistance to reduction with metals and acids or sodium and alcohol eliminated the grouping $—N{=}C<$. Acetylation proceeded readily, and a diacetyl derivative (V) was iso-

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(1) National Research Council Fellow.

(2) Troeger, *J. prakt. Chem.*, [2] **36**, 227 (1887).

(3) Löb, *Z. Elektrochem.*, **4**, 428 (1898).

(4) Goecke, *ibid.*, **9**, 470 (1903).

(5) Lepetit and Maimeri, *Atti accad. Lincei*, [5] **26**, 558 (1917); Lepetit, Maffei and Maimeri, *Gazz. chim. ital.*, **57**, 862 (1927).

(6) Eisner and Wagner, THIS JOURNAL, **56**, 1938 (1934).