tures, (3) the constancy of the vapor pressure at 0 and −31.2° after severe fractionation, (4) the sharp melting point, (5) the excellent agreement of the analysis with that demanded for dimethylacetylene.

Summary

Pure dimethylacetylene has been synthesized and its isolation has been simplified. The vapor pressure at several temperatures, between the melting and boiling points, has been determined and the data have been fitted to an equation. The refractive index was measured at 25° and the density was determined at 0 and 25°. The boiling point and freezing point lie within 60° of each other.

MINNEAPOLIS, MINN. RECEIVED AUGUST 6, 1934

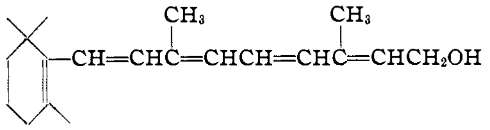
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Synthesis of Certain Unsaturated Compounds from Beta-Ionone and Tetrahydroionone[1,2,3]

BY R. G. GOULD, JR., AND A. F. THOMPSON, JR.

In 1931 Karrer[4] put forward a structural formula for vitamin A (I) based on a study of

I



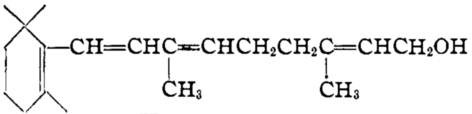
highly active fish liver oils. This formula is supported by further work on liver oil concentrates[5] and by the synthesis of perhydrovitamin A.[6] No compounds with vitamin A activity have as yet been synthesized. This would seem to be particularly important inasmuch as the most active concentrates of fish liver oils are admittedly not pure, and no solid derivatives of the vitamin have been obtained.

Ruzicka[7] has synthesized a tetrahydrovitamin A and found it to be biologically inactive.

Karrer[8] has prepared from β-ionone by means of the Reformatsky reaction 2-methyl-4-(2,2,6-trimethylcyclohexenyl-Δ^6)-butadiene-1,3-carboxylic acid, and has also synthesized two highly unsaturated ketones[9] which, however, do not have a carbon skeleton related to that assigned to vitamin A.

Synthesis of the partial reduction products of vitamin A is of interest in connection with the question as to the ability of the animal body to dehydrogenate such compounds to form active vitamin A, and also with the possible vitamin A activity of β-dihydrocarotene. Von Euler[10] has claimed that this compound, prepared by reduction of β-carotene with aluminum amalgam, is somewhat active, but Drummond[11] believes that the activity is entirely due to unchanged β-carotene present as an impurity.

In the work reported in this paper we have achieved the first steps in a projected synthesis of a dihydrovitamin A (II), and also have made progress



II

toward an independent synthesis of perhydrovitamin A. The compounds which we have prepared so far are given in the diagram.

The condensation of acetylene with β-ionone and with tetrahydroionone was carried out by a modification of the reaction developed by Ruzicka[12] and used by Rupe,[13] and F. G. Fischer.[14] These authors used sodamide or metallic sodium as condensing agent; the reaction often goes with great difficulty, and in many cases the yield is

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(1) Part of the material presented here was used in the doctoral theses of both authors.

(2) The authors take great pleasure in acknowledging their indebtedness to Dr. James B. Conant, who suggested the problem and directed the greater part of the work, and to Professor E. P. Kohler for criticisms and suggestions in connection with writing this paper.

(3) The ionone used was kindly furnished us by E. I. du Pont and Company.

(4) Karrer, Morf and Schopp, *Helv. Chim. Acta*, **14**, 1036 (1931); **14**, 1431 (1931).

(5) Heilbronn, Heslop, Morton, Webster, Rea and Drummond, *Biochem. J.*, **26**, 1178 (1932).

(6) Karrer and Morf, *Helv. Chim. Acta*, **16**, 557 (1933); **16**, 625 (1933).

(7) Ruzicka and Fischer, *ibid.*, **17**, 633 (1934).

(8) Karrer, Salomon, Morf and Walker, *ibid.*, **15**, 878 (1932).

(9) Karrer and Morf, *ibid.*, **17**, 3 (1934).

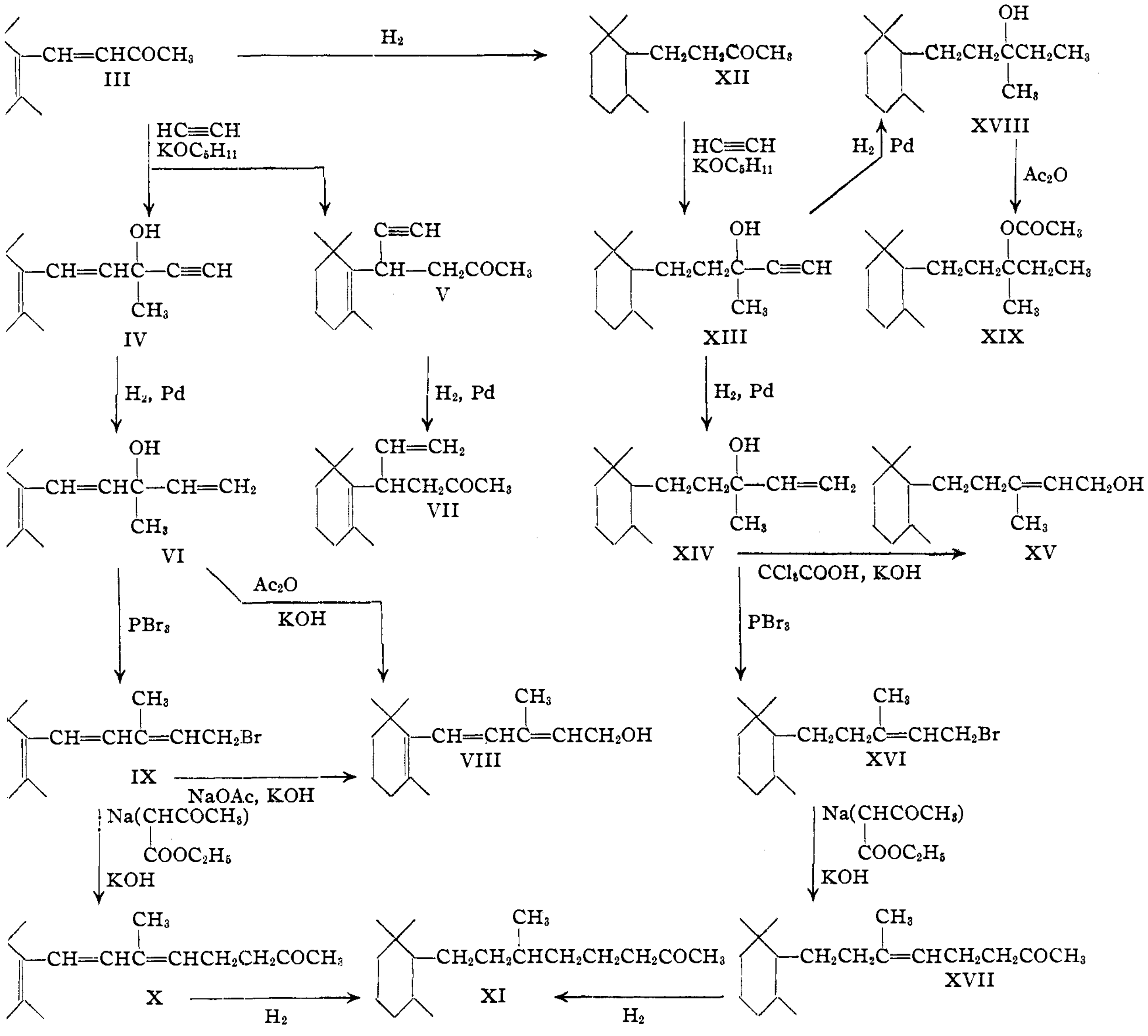
(10) Von Euler, Karrer, Helstrom and Rydbom, *Svensk. Kem. Tidskr.*, **43**, 105 (1931).

(11) Drummond, *J. Soc. Chem. Ind.*, **50**, 183T (1931).

(12) Ruzicka and Fornasir, *Helv. Chim. Acta*, **2**, 182 (1919); Ruzicka, *ibid.*, **6**, 493 (1923).

(13) Rupe and Kambli, *ibid.*, **9**, 672 (1926); Rupe, Messner, and Kambli, *ibid.*, **11**, 449 (1928); Rupe and Giesler, *ibid.*, **11**, 656 (1928); Rupe, Wirz and Lotter, *ibid.*, **11**, 965 (1928); Rupe and Hirschmann, *ibid.*, **14**, 687 (1931).

(14) F. G. Fischer and Lowenberg, *Ann.*, **475**, 183 (1929).



poor. We have found that by using potassium *t*-amylate or *t*-butylate as condensing agent, saturated ketones such as tetrahydroionone react with acetylene rapidly in the cold and give yields as high as 80%. *β*-Ionone could not be condensed with acetylene when sodamide was used as condensing agent due to the fact that it does not react with sodamide alone, even on heating for several hours; with potassium *t*-amylate, however, it gives a mixture of approximately equal amounts of the normal 1,2 addition product (IV) and some other acetylenic compound, which we have tentatively designated as the 1,4 product (V).

All the evidence we have obtained on the physical and chemical properties of the reaction product is consistent with this assumption. The hydrogenation value, semi-quantitative analyses for hydroxyl groups and Zerewitinoff analysis all indicated 50–55% of a hydroxyl compound.

However, the main evidence for the structure of the 1,2 addition product is based on the rest of the synthesis. No crystalline derivatives of the acetylenic compounds were obtained.

Partial reduction of the acetylenic compounds to the corresponding ethylenes[14] proceeded smoothly in both the *β*-ionone and tetrahydroionone series, since the products showed less than 5% of acetylenic material after the absorption of one mole of hydrogen.

The unsaturated primary alcohol VIII was obtained by rearrangement of the tertiary alcohol

VI with acetic anhydride and also by formation of the primary bromide VII with phosphorus tribromide and subsequent condensation with sodium acetate. Both methods gave very small yields; the material was isolated and characterized as the phthalic acid ester.

The primary alcohol XV was obtained from XIV in good yields by treatment with trichloroacetic acid (60% yield) or acetic anhydride (20% yield). The latter reagent did not give reproducible results.

Transformations of secondary and tertiary vinyl carbinols to the corresponding primary bromides are well known.[15,16,17]

We have prepared the primary mono-unsaturated bromide (XVI) from both the tertiary alcohol (XIV) and the primary alcohol (XV), and have found that slightly better yields of bromide are obtained by direct bromination of the tertiary compound than by going through Compound XV. The bromide could not be purified since it decomposed on distillation, but its structure was proved by condensation with sodium acetoacetic ester, followed by ketone cleavage giving the mono-unsaturated ketone XVII, the structure of which was proved definitely. This ketone gave a crystalline semicarbazone and on catalytic reduction it took up one mole of hydrogen to give the saturated ketone XI, first prepared by Karrer.[6]

In the β-ionone series, the mixture of partially reduced 1,2 and 1,4 products on treatment with phosphorus tribromide gave the primary bromide IX from the 1,2 product, the 1,4 product remaining unchanged as it did not contain a hydroxyl group. After condensation with sodium acetoacetic ester and cleavage, the triply unsaturated ketone X was obtained in pure condition by distillation, as it has a considerably higher boiling point. This ketone gave a crystalline semicarbazone, and on catalytic reduction it took up three moles of hydrogen to give the saturated ketone XI. The identity of the saturated ketones obtained from the β-ionone and the tetrahydroionone series was shown by the mixed melting points of the semicarbazones.

Experimental Part

1. **Purification of β-Ionone (III).**—The β-ionone kindly furnished by du Pont and Company contained about 80% β-ionone, 10% α-ionone and 10% terpenes. It was purified by fractional crystallization of the sodium bisulfite compound. After two fractional distillations the properties were $n^{24}{}_{\rm D}$ 1.5202.

2. **Tetrahydroionone (XII)** was prepared by reduction of ionone in glacial acetic acid solution. After fractionation in vacuum, the ketone gave a semicarbazone, m. p. 183–184°. The properties of the ketone were $n^{23}{}_{\rm D}$ 1.4697, $d^{23}{}_4$ 0.9043, $M_{\rm D}$ found 60.49; calcd. 60.04.

3. **3-Hydroxy-3-methyl-5-(2,2,6-trimethylcyclohexenyl-Δ^6)-penten-4-ine-1 (IV)** was obtained by condensation of acetylene with β-ionone: 250 g. of anhydrous ether was cooled to −15° and saturated with dry, purified acetylene gas. A solution of 250 g. of β-ionone in about 250 g. of anhydrous ether and a solution of 50 g. of potassium dissolved in 600 cc. of anhydrous *t*-amyl alcohol were added separately to the ether solution of acetylene, with good mechanical stirring, over a period of about two hours. Acetylene was passed in during the addition of the reactants and for four to six hours afterward, and the mixture was cooled to −10–15° during the addition and kept at 0° afterward. The reaction mixture was decomposed by shaking with a small excess of dilute ice-cold hydrochloric or sulfuric acid solution, and worked up in the usual manner. On distillation in a vacuum, about 50 g. of product was obtained as a light yellow oil, boiling at 115–125° at 2–3 mm. On redistillation, the material boiled at 114–117° at 2 mm.; $n^{24}{}_{\rm D}$ 1.5063, $d^{24}{}_4$ 0.9468, $M_{\rm D}$ found 68.43.

Anal. Calcd. for $C_{15}H_{22}O$: C, 82.5; H, 10.1. Found: C, 81.98, 81.64; H, 10.17, 10.06.

All the compounds in the β-ionone series were found to be autoxidizable and hence were always stored in an atmosphere of nitrogen. All reactions and distillations were carried out in an inert atmosphere. It should be mentioned that the refractive index of the product depends to a certain extent on the length of time of the acetylene condensation. As it was difficult to determine the purity of the acetylenic compound accurately, we ordinarily used eight hours for the total time of condensation, even though this cut down the yield considerably, so as to be sure of obtaining a product reasonably free of unchanged β-ionone.

Hydrogenation Value.—1.008 grams of product, 0.05 g. of Adams catalyst and 15 cc. of glacial acetic acid absorbed 402 cc. of hydrogen or 3.52 mols.

Zerewitinoff Analysis.—A small sample of product was saturated with hydrogen in the presence of Adams catalyst, distilled, and dried by standing over sodium overnight: 0.58 mol gave 0.34 m. mol of gas; calcd. for a mixture of 50% 1,2 and 50% 1,4 products, 0.29 m. mol.

Purification through Silver Salt.—The silver salt was obtained by treating a solution of the acetylenic compound in methanol with methyl alcoholic ammoniacal silver nitrate. The light yellow, non-crystalline precipitate was filtered, washed with alcohol–water mixture and with alcohol, and dried. It is very explosive when dry and tends to become oily. It was dissolved in ether and treated with dilute hydrochloric acid solution. The ether solution was worked up in the usual manner, giving a yield of about 20% of acetylenic compound practically unchanged in physical properties.

4. **3-Hydroxy-3-methyl-5-(2,2,6-trimethylcyclohexyl)-pentine-1 (XIII)** was obtained by condensation of acetylene

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(15) Prévost, *Ann. chim.*, [10] **10**, 123 (1928).

(16) Karrer and Helfenstein, *Helv. Chim. Acta*, **14**, 78 (1931).

(17) Rambaud, *Compt. rend.*, **195**, 389 (1932).

with tetrahydroionone. This condensation takes place in the presence of sodamide, but it was found that potassium *t*-amylate was a superior condensing agent in that it decreased the time of reaction 75% and improved the yield of acetylenic compound. The same conditions were used in this condensation as in the case of β-ionone. The product was obtained as an extremely viscous, very pale yellow oil, boiling at 117–118° (2 mm.). The yield of nearly pure material after fractionation was 80%. The properties of this compound were n^{23}_D 1.4802, d^{23}_4 0.9189, M_D found 68.72; calcd. 68.91.

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.0; H, 11.7. Found: C, 80.8, 81.34; H, 11.83, 11.76. *Hydrogenation value.* 5.331 g. absorbed 1100 cc. of H_2 or 2.04 mols; calcd. 2.0 mols.

5. **3-Hydroxy-3-methyl-5-(2,2,6-trimethylcyclohexyl)-pentane (XVIII)** was obtained by hydrogenation of the corresponding pentine (XIII) in glacial acetic acid solution with Adams catalyst. The saturated alcohol was obtained in practically quantitative yield as a colorless oil, somewhat less viscous than the acetylenic compound. The properties of this compound were: b. p. 112–113° (2 mm.), n^{24}_D 1.4740, d^{24}_4 0.9039, M_D found 70.38; calcd. 70.91.

Anal. Calcd. for $C_{15}H_{30}O$: C, 79.6; H, 13.3. Found: C, 79.64, 79.84; H, 13.07, 12.6.

The acetate XIX corresponding to the carbinol XVIII was obtained from the tertiary carbinol by heating it with twice the theoretical amount of acetic anhydride at 100° for 120 hours. The yield of ester was about 20%. The ester was a colorless mobile liquid: b. p. 124–125° (2 mm.), n^{22}_D 1.4630, d^{22}_4 0.9223, M_D found 80.12; calcd. 80.04.

Anal. Calcd. for $C_{17}H_{32}O_2$: C, 76.1; H, 12.0. Found: C, 76.1, 76.63; H, 11.7, 11.67.

6. **3-Hydroxy-3-methyl-5-(2,2,6-trimethylcyclohexenyl-Δ^6)-pentadiene-1,4 (VI)** was prepared by the partial reduction of the corresponding acetylenic compound (IV). The palladium catalyst is that described by Busch and Stowe.[18]

We have found that the acetylenic compounds take up very nearly 1 mole more hydrogen in glacial acetic acid than in methyl or ethyl alcohol, and have accordingly always used glacial acetic acid for complete reductions and alcohol for partial ones.

Since the mixture of acetylenic compounds is never quite free from non-acetylenic material, the hydrogen uptake just sufficient to abolish the ammoniacal silver nitrate test is determined on a series of small samples. A sharp change in slope of the hydrogenation curve was often obtained at about 0.90 mol, confirming the assumption that the reduction proceeds in clear-cut stages.

Analysis for OH Groups.—5.0 grams of freshly distilled product and 10 cc. of phenyl isocyanate were allowed to stand overnight, protected from the air, and then heated to 100° for two to three hours, and 200 cc. of dry petroleum ether (b. p. 30–50°) added and allowed to stand for several hours. The precipitate of diphenylurea was filtered and washed with petroleum ether: calcd. for a mixture of 50% 1,2 and 50% 1,4 products 2.66 g.; found, 2.45 g.

7. **3-Hydroxy-3-methyl-5-(2,2,6-trimethylcyclohexyl)-pentene-1 (XIV)** was obtained in the same manner from the corresponding ethylenic compound XIII. Adams catalyst was tried and found to give a less homogeneous product. The properties of the ethylenic carbinol were: b. p. 115–116° (2 mm.), n^{24}_D 1.4788, d^{24}_4 0.9074, M_D found 70.44; calcd. 70.04.

8. 3-Methyl-5-(2,2,6-trimethylcyclohexenyl-Δ^6)-pentadien-2,4-ol-1 (VIII)

(a) **Acetic Anhydride Method.**—The directions of Ruzicka[12] and of F. G. Fischer[14] were used. The conditions tried were 100° for ninety hours, with and without small amounts of sodium acetate, and refluxing at 138° for nine hours. On fractionation in vacuum, there was no constant boiling primary acetate fraction, but the higher boiling fractions were saponified with dilute methyl alcoholic potash and distilled. The high boiling fraction was treated with phthalic anhydride, and the phthalic acid half ester isolated according to the directions given for farnesol phthalate by Ruzicka.[12] The ester was a light brown oil, so viscous as to be immobile at room temperature.

Anal. Calcd. for $C_{23}H_{28}O$: C, 75.0; H, 7.6. Found: C, 75.6, 76.0; H, 8.4, 8.8. *Titration value.* 0.2555 mg. required 6.21 cc. of 0.106 *N* base. Calcd. 0.694 m. mols; found, 0.658.

Hydrogenation Value.—0.3005 gram of ester absorbed 73 cc. of hydrogen: calcd. for 3 mols., 64.8 cc. Some phthalic acid precipitated out during the reduction, thus accounting for the excess of hydrogen consumed. This is not unexpected since many α,β unsaturated primary alcohols (and esters) on catalytic hydrogenation are known to give saturated hydrocarbons and water (or free acids).[19]

(b) **Trichloroacetic Acid Method.**—The only conditions tried with this reagent were mixing the ethylenic tertiary alcohol with the same weight of trichloroacetic acid dissolved in twice the weight of glacial acetic acid at room temperature and allowing to stand for four to five hours. The results were substantially the same as with the acetic anhydride method.

9. **3-Methyl-5-(2,2,6-trimethylcyclohexyl)-penten-2-ol-1 (XV)** was obtained from the corresponding tertiary compound (XIV) by rearrangement through the acetate or trichloroacetate. The trichloroacetate gave much better results, since yields of 55% could usually be obtained.

The tertiary carbinol (XIV) was mixed with an equimolecular amount of trichloroacetic acid dissolved in twice its weight of glacial acetic acid and heated at 65° for five hours. The ester was not isolated, but after washing free from acid it was refluxed for four hours with excess methyl alcoholic potash. The saponification product was fractionated, the fraction from 125–130° consisting of 90% pure primary alcohol (XV). The yield was 50–60%; b. p. 125–126° (2 mm.), n^{20}_D 1.4926, d^{20}_4 0.9283, M_D found 70.14; calcd. 70.44.

Anal. Calcd. for $C_{15}H_{28}O$: C, 80.2; H, 12.5. Found: C, 80.25, 79.95, 80.14; H, 13.02, 12.05, 13.05.

The over-all yield of this compound from tetrahydroionone is 40%. A phthalic acid ester was prepared from

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[18] Busch and Stowe, *Ber.*, **49**, 1064 (1916).

[19] Willstätter and Mayer, *ibid.*, **41**, 1475 (1908).

this compound according to Ruzicka's method with farnesol. Like farnesol, it did not give any crystalline derivatives but could be freed from non-acidic materials by transferring from ether to water solution and then back to ether, and from phthalic acid by extraction of a benzene solution with water, since phthalic acid is sparingly soluble in benzene.

Anal. Calcd. for $C_{23}H_{30}O_4$: C, 74.6; H, 8.60. Found: C, 74.57, 74.70; H, 8.72, 8.90. *Neutral equivalent* (phenolphthalein). 2.520 g. of ester required 8.10 cc. of 0.868 N NaOH; calcd., 7.84 cc. *Saponification value.* 2.520 g. of ester required 8.2 cc. of 0.868 N NaOH; calcd., 7.84 cc.

The physical properties given above were obtained on a sample of alcohol regenerated from the phthalic acid ester by boiling for six hours with 20% alcoholic potash.

10. 1-Bromo-3-methyl-5-(2,2,6-trimethylcyclohexenyl-Δ^6)-pentadiene-2,4 (IX).—The mixture of ethylenic compounds was treated with phosphorus tribromide by the method of Kirrmann,[20] following the directions of Karrer[21] for nerolidol. The quantities of reagents used were calculated on the assumption that the mixture contained 50% of an alcohol.

On working up the reaction mixture, three layers were obtained. The layer in between the ether and aqueous layer proved to be a viscous dark oil, with a low bromine content. When dissolved in a large quantity of ether, it could be extracted by sodium bicarbonate solution. This material was discarded.

The bromide was obtained as a reddish oil, much less viscous than the alcohol. It decomposed on heating in a vacuum and slowly on standing, and was used as soon after being prepared as possible. The ether solution of the bromide was dried with calcium chloride and the ether evaporated off in vacuum, the last traces being removed by warming and evacuating with an oil pump. It was analyzed by the Stepanov method, which did not give a sharp end-point, and by direct saponification with methyl alcoholic potash.

Anal. 1.495 g. of bromide mixture neutralized 5.37 cc. of 0.530 N KOH. Calcd. for $C_{15}H_{23}Br$: Br, 28.3. Found: Br, 15.3.

11. 1-Bromo-3-methyl-5-(2,2,6-trimethylcyclohexyl)-pentene-2 (XVI).—This bromide was prepared from the corresponding mono-unsaturated primary alcohol (XV), and from the tertiary alcohol (XIV) in exactly the same manner as described above. In both these cases the viscous intermediate layer was obtained.

Anal. (Stepanov). 0.469 g. of bromide required 14.0 cc. of 0.1 N $AgNO_3$. Calcd. for $C_{15}H_{27}Br$: Br, 27.9. Found: Br, 23.9.

We obtained a yield of 70%. No proof of the structure of this bromide can be afforded since it could not be distilled. but it reacts as a primary bromide in the next stage of the synthesis.

Under the same conditions, 50 g. of the primary carbinol, XV, yielded 60 g. of a product containing 93% of the theoretical amount of Br.

Anal. (Stepanov). 0.693 g. of bromide required 22.5 cc. of 0.1 N $AgNO_3$ soln. Calcd. for $C_{15}H_{27}Br$: Br, 27.9. Found: Br, 26.0.

This corresponds to a 90% yield. Since the yield of primary alcohol by trichloroacetate rearrangement was 60%, this is a 54% over-all yield from the tertiary alcohol XIV. Direct bromination of the alcohol XIV is thus more advantageous.

12. 6-Methyl-8-(2,2,6-trimethylcyclohexenyl-Δ^6)-octadien-5,7-one-2 (X).—This triply unsaturated ketone was prepared by condensation of the bromide IX with sodium acetoacetic ester and subsequent cleavage with dilute alkali.

In 300 g. of absolute ethyl alcohol dried over magnesium methylate was dissolved 5 g. of metallic sodium. The solution was cooled to −10° and 45 g. of pure acetoacetic ester was added. A solution of 35 g. of the bromide preparation which contained about 18–20 g. of the bromide IX dissolved in 100 cc. of dry petroleum ether was then added, the temperature being maintained at −10° during the addition and for one hour afterward. The mixture was then allowed to warm to room temperature during another hour, and finally refluxed for one hour. After cooling enough 5% methyl alcoholic potash solution to saponify the acetoacetic ester originally present was added (0.4 mol.); the mixture was allowed to stand overnight and was then refluxed for one hour, and the low boiling solvents distilled off in a vacuum. The residue was taken up in a large volume of ether and washed with water until the water washings were neutral to litmus (2–3 liters). On distillation, 6 g. of material boiling at 163–168° (3 mm.) was obtained. On redistillation it boiled at 165–168° (3 mm.), and the refractive index was $n^{19}\text{D}$ 1.5210.

Hydrogenation value. 2.385 g. of ketone absorbed 605 cc. of hydrogen at 25° or 2.94 mols.

Semicarbazone.—Good yields of a crystalline semicarbazone were readily obtained, which after several recrystallizations from methanol and from benzene–petroleum ether mixture melted at 160–160.5°.

Anal. Calcd. for $C_{19}H_{31}N_3O$: C, 71.9; H, 9.85; N, 13.24. Found: C, 72.15, 71.99; H, 10.09 (9.39); N, 13.5.

13. 6-Methyl-8-(2,2,6-trimethylcyclohexyl)-octene-5-one-2 (XVII).—The preparation of this mono-unsaturated ketone in identical yields from bromides derived independently from the tertiary alcohol (XIV), and the primary alcohol (XV), affords complete proof of the structural identity of these two bromide samples.

The directions above for the condensation and cleavage were followed except that the quantity of bromide used was 50% as great, since these bromides are pure. On distillation, the ketone was collected at 165–168° (3 mm.). The yield was 45% in either case, and the physical properties for the two preparations were the same: $n^{24}\text{D}$ 1.4810, $d^{24}{}_4$ 0.9026. M_D found 83.37, calcd. 82.67.

Hydrogenation value. 0.959 g. of ketone absorbed 99 cc. of H_2, or 0.99 mol; calcd. 1.0 mol.

The semicarbazone crystallized readily and in good yield. It melted at 133° after several recrystallizations from methyl alcohol.

Anal. Calcd. for $C_{19}H_{35}N_3O$: C, 71.0; H, 10.98; N, 13.09. Found: C, 71.26, 70.82; H, 11.22, 10.81; N, 13.28, 13.32.

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(20) Kirrmann, *Bull. soc. chim.*, [4] **39**, 698 (1926).

(21) Karrer, *Helv. Chim. Acta*, **14**, 82 (1931).

14. 6-Methyl-8-(2,2,6-trimethylcyclohexyl)-octanone-2 (XI).—This saturated ketone was prepared from the mono-unsaturated ketone XVII, and from the triunsaturated ketone X, by catalytic hydrogenation.

(a) Twenty-seven grams of mono-unsaturated ketone and 0.10 g. of Adams catalyst in glacial acetic acid solution absorbed the calculated amount of hydrogen in sixty-five minutes. After distillation the physical properties were: n^{24}_{D} 1.4690, d^{24}_{4} 0.8896, M_D found 83.34, calcd. 83.14.

The semicarbazone after recrystallization from methyl alcohol melted at 113.5°. Karrer gives 113.5–114° for this compound.

Anal. Calcd. for $C_{19}H_{37}N_3O$: C, 70.6; H, 11.53; N, 13.00. Found: C, 70.65, 70.75; H, 11.33, 11.30; N, 12.76, 12.63.

(b) 2.38 g. of tri-unsaturated ketone X, and 0.05 g. of Adams catalyst in 30 cc. of glacial acetic acid absorbed 605 cc. of hydrogen in about ten hours. The material was fractionated into two fractions, both of which gave good yields of a semicarbazone melting at 113.5–114°; mixed m. p. with that above was 113.5–114°.

Summary

This paper describes the preparation in five steps of 6-methyl-8-(2,2,6-trimethylcyclohexenyl-Δ^6)-octadien-5,7-one-2 from β-ionone, and the corresponding 6-methyl-8-(2,2,6-trimethylcyclohexyl)-octanone-2 from tetrahydroionone. The initial step in the synthesis, addition of acetylene to the ketones, was accomplished using potassium *t*-amylate as condensing agent. This is a new reaction in the case of β-ionone, an α,β-unsaturated ketone; and in the case of tetrahydroionone resulted in a faster reaction and improved yields for the acetylene condensation. The 6-methyl-8-(2,2,6-trimethylcyclohexenyl-Δ^6)-octadien-5,7-one-2 is of special interest as an intermediate in our projected synthesis of dihydrovitamin A.

RECEIVED SEPTEMBER 4, 1934

[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY, NEW YORK STATE AGRICULTURAL EXPERIMENT (GENEVA) STATION]

Water Relations of Enzymes. I. Influence of Viscosity on Invertase Action[1]

BY Z. I. KERTESZ

Because the importance of water in biological reactions has been much emphasized recently, an investigation of water relations of enzymes was undertaken; and since much information was available on invertase and its kinetics, this enzyme was selected for the work. The present paper deals with the influence of viscosity on the rate of sucrose inversion by invertase.

Achalme and Bresson[2] and later Colin and Chaudun,[3] claimed that the viscosity is a governing factor in enzyme reactions and that the rate of sucrose inversion by invertase is proportional to the fluidity of the medium. Schubert[4] and Nelson and Schubert[5] showed the faultiness of this assumption. According to the latter authors the concentration of water is a factor determining the rate of inversion. Auden and Dawson[6] were also unable to confirm the findings of the French authors.

In all the experiments of the above workers high concentrations of sucrose, glycerol and alcohol were used to alter the viscosity of the medium. This method is not entirely satisfactory in a study of the influence of viscosity because of the great changes that are produced in the concentration of the water and possible inhibiting action of glycerol and alcohol. Colin and Chaudun[7] determined the rate of inversion in the presence of gelatin and gelose and again found the previously claimed relation between fluidity and velocity of the reaction. Several serious objections might be raised to their work, however. First, the determination of changes of optical rotation in sucrose–gelatin mixtures is uncertain and has been found unworkable by the author. Second, a partial solidification of the gelatin sols might introduce serious changes in the velocity of the reaction, as shown by Freiberger[8] for amylolysis. Third, gelatin itself has been found by Filipowicz[9] to influence enzyme action (amylolysis) greatly. Finally, the whole range of viscosity change was very small, that of the medium being only doubled by the added materials.

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(1) Approved by the Director of the New York State Agricultural Experiment Station for publication as Journal Article No. 46. Presented at the "Symposium on the Chemistry of Enzymes" at the Cleveland meeting of the American Chemical Society, Sept. 12, 1934.

(2) Achalme and Bresson, *Compt. rend.*, **152**, 1328, 1420, 1621 (1911).

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