[Contribution from the Chemical Laboratory of Northwestern University]

The Degradation of Alkenyltrimethylammonium Hydroxide

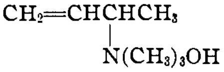
By Charles D. Hurd and Elwood H. Ensor

In Willstätter's synthesis of cyclooctatetraene from pseudopelletierine, double bonds were introduced by the Hofmann degradation method. The steps involved were reasonable if it was assumed that each new double bond was conjugate, not cumulative.

To throw light on the validity of this assumption, Hurd and Drake[1] prepared and pyrolyzed 2,3-butanebis-(trimethylammonium hydroxide), $(CH_3{-}CH(NMe_3OH){-})_2$. 1,3-Butadiene was indeed formed, but isomeric material (1,2-butadiene or 2-butyne) was formed in still larger amounts. It was established, therefore, that the Hofmann degradation does not necessarily lead to the formation of conjugate double bonds. On the basis of this evidence it was questioned whether or not the cyclooctatetraene contained double bonds exclusively.

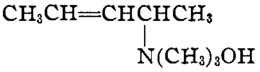
Hurd and Drake's experiment differed from Willstätter's, however, in an important particular. It started with a molecule containing two quaternary ammonium functions and no double bond, whereas Willstätter's started with a molecule containing one quaternary ammonium function and a double bond. Hence it could be argued that the preëxisting double bond might direct the incoming double bond to a conjugated position. The present investigation was undertaken to seek an answer to this question.

The simplest model compound would be (1-methylallyl)-trimethylammonium hydroxide (I). It, however, or the halide from which it would be



$$CH_2{=}CH\underset{\substack{|\\N(CH_3)_3OH}}{C}HCH_3$$

I



$$CH_3CH{=}CH\underset{\substack{|\\N(CH_3)_3OH}}{C}HCH_3$$

II

made, suffers from uncertainty as to structure because of the allylic system. No such uncertainty would appear with (1-methylcrotyl)-trimethylammonium hydroxide (II); hence it was selected for study. 2,3-Pentadiene would result if cumulative double bonds of the allene type were produced in the Hofmann degradation, and 1,3-pentadiene if conjugated double bonds were formed.

Crotonaldehyde was the starting point for the synthesis of II. Its reaction with methylmagnesium iodide yielded 3-pentenen-2-ol only if water was the hydrolyzing agent. Hydrolysis by dilute sulfuric acid produced chiefly 1-methylcrotyl ether, an observation noted earlier by Boudringhien.[2] Conversion of the unsaturated alcohol into its bromide was carried out using Mulliken's directions,[3] the chief feature of which is to avoid long duration of contact of the alcohol with hydrobromic acid; otherwise addition of hydrogen bromide occurs also at the double bond.

Instead of adding to 3-bromo-2-pentene to produce the quaternary salt, pure trimethylamine caused detachment of the elements of hydrogen bromide; but a smooth addition was effected in the presence of dioxane. Final conversion of the bromide into II was effected by shaking it for several hours with a mixture of silver oxide and water.

trans-1,3-Pentadiene is absorbed quantitatively in molten maleic anhydride whereas the *cis* isomer is unabsorbed.[4,5] 2,3-Pentadiene, of course, would be unaffected by maleic anhydride. Obviously, therefore, the analytical problem would be simplified if the *trans* diene was the exclusive or nearly exclusive product from the pyrolysis of II. An alternative method, suitable for analyzing 2,3-pentadiene if present in substantial amounts is analytical distillation, since the *trans* diene[5] boils at 42°, the *cis* at 43.5°, and the 2,3-isomer[6] at 49–51°.

Two different samples of 1,3-pentadiene were obtained in preliminary work. One boiling at 42° was formed as the chief product of reaction between crotonaldehyde and methylmagnesium iodide when an excess of Grignard reagent was taken. This hydrocarbon was 95–96% absorbed in maleic anhydride, pointing to the *trans* diene. Whether the remaining 4–5% was *cis* diene or some other material cannot be stated. The other source of 1,3-pentadiene was by cleavage of the 1-methylcrotyl ether, mentioned above, with hydrobromic acid. This diene, of b. p. 41–42°, was 100% absorbed in maleic anhydride, which suggested that its structure was completely *trans*. A mixture of this diene (51%) and 2-pentene (49%) gave analytical figures of 52% diene and 48% pentene, pointing to an accuracy of about 1% in this analysis.

The pentadiene obtained by pyrolysis of II was absorbed to the extent of 95–96% in maleic anhydride, showing that at least 95–96% of this hydrocarbon is the *trans* diene. The rest may have been the *cis* diene; at least, no evidence for the higher boiling 2,3-pentadiene could be obtained by distillation analysis through a precision column.

This finding supports Willstätter's claim for the formation of conjugated structures in his synthesis of cyclooctatetraene. The structure of the latter has been amply verified in recent

---

[1] Hurd and Drake, This Journal, **61**, 1943 (1939).

[2] Boudringhien, *Bull. sci. acad. roy. Belg.*, **15**, 53 (1929).

[3] Mulliken, This Journal, **57**, 1605 (1935).

[4] Robey, Morrell and Wiese, *ibid.*, **63**, 627 (1941); Frank, Emmick and Johnson, *ibid.*, **69**, 2313 (1947).

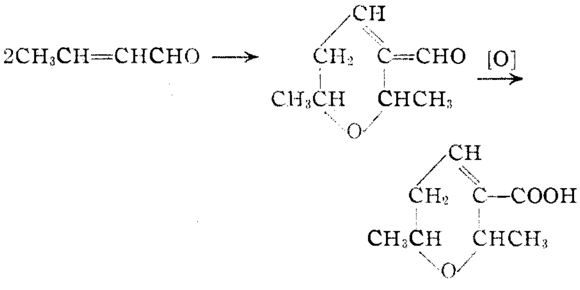
[5] Craig, *ibid.*, **65**, 1006 (1943); **72**, 1678 (1950).

[6] Kukuritschkin, *J. Russ. Phys.-Chem. Soc.*, **35**, 873 (1903).

years, especially by Cope's[7] confirmation of Willstätter's synthesis.

Some experiments were performed also on the reaction of 1,4-dichloro-2-butene with trimethylamine. Methods were found for introducing either one or two moles of amine into reaction. Use of dioxane as solvent restricted the reaction so that one mole was introduced, whereas use of methanol as solvent brought about the further reaction with two moles.

It is known[8] that octatrienal, $CH_3CH{=}CHCH{=}CHCH{=}CHCHO$, is formed in the aldol condensation of crotonaldehyde. It was hoped that this could be made to undergo a vinylogous intramolecular aldol condensation to yield 2,4,6-cycloöctatrienol from which cycloöctatetraene should be readily obtainable. High dilution methods seemed a promising approach, hence crotonaldehyde and sodium methoxide were placed in reaction at high dilution in methanol. No cycloöctatrienol was found, but a small yield of 2,6-dimethyl-5,6-dihydro-3-pyrancarboxylic acid[9] was isolated



Experimental Part

3-Penten-2-ol.—Reif's directions[10] were followed, using crotonaldehyde (1.5 moles) and methylmagnesium halide (1.48 moles). At the end of the reaction, ether was distilled off and the resulting liquid was poured into a mixture of ice and water.[2] Steam distillation, separation and drying of the alcohol layer, and distillation yielded 58 g. (61%) of 3-penten-2-ol, b. p. 120–124°.

Variations.—If the above reaction mixture was hydrolyzed by pouring it into a beaker of ice and dilute sulfuric acid, ice being present continuously, a different result was observed. The organic layer was ether extracted, washed with sodium bicarbonate and bisulfite solutions and finally with water, and then dried. Distillation yielded only 3.7 g. of 3-penten-2-ol, b. p. 122–124°, but 36.5 g. of 1-methylcrotyl ether, b. p. 158°.

If 1.7 moles (not 1.48) of Grignard reagent in the above example was treated with 1.5 moles of crotonaldehyde, the isolated yield of 26–27 g. of 3-penten-2-ol (b. p. 71–74° (36 mm.)) was accompanied with 12–13 g. of 1,3-pentadiene, b. p. 42°.

Reaction of 4-Bromo-2-pentene with Trimethylamine.—4-Bromo-2-pentene,[3] b. p. 70–73° (145 mm.), was obtained in 50% yield by shaking 40 g. of 3-penten-2-ol for twenty minutes with 35 g. of 48% hydrobromic acid, separating the layers and shaking the organic layer for twenty minutes more with 18 g. of fresh acid. Much 1-methylcrotyl ether was formed also.

Precipitation started soon after mixing 41 g. of 4-bromo-2-pentene, 200 g. of dry dioxane and 40 g. of liquid trimethylamine. Excess amine was distilled off after fifteen hours at room temperature. The white salt was collected on a filter. It was very soluble in butanol and ethanol, from which solutions it tended to separate as an oil on addition of dioxane. The salt was crystallized from absolute alcohol; m. p. 171.2–171.5°. Yields in several experiments were 75–80%.

Anal. Calcd. for $C_8H_{18}BrN$: Br, 38.44. Found: Br, 38.47.

Without solvent, 4-bromo-2-pentene and trimethylamine reacted at 0° to yield trimethylammonium bromide. Similarly, pyridine (at 20°) and morpholine rapidly yielded their crystalline hydrobromides, but the comparable reaction with dimethylaniline was very slow and incomplete without formation of crystals.

1,3-Pentadiene from 1-Methylcrotyl Ether.—Boudringhien[2] mentioned this reaction but listed no details or yields.

About 90–100 g. of 48% hydrobromic acid was added dropwise into a flask containing 58 g. of 1-methylcrotyl ether (of b. p. 158°) which was heated by an oil-bath at 130–133°. Reaction was interrupted when half of the ether layer had disappeared. The organic top layer (55 g.) of the distillate, after washing with water and sodium carbonate solution and drying, was separated by two distillations into 13 g. of 1,3-pentadiene, b. p. 41–42°, 15 g. at 115–125° which was chiefly 4-bromo-2-pentene, and 5 g. of original ether.

A middle cut of this pentadiene possessed these constants: b. p. 41.9°, d^{26}_4 0.673, n^{20}_D 1.4320. As will be seen, this sample was completely soluble in maleic anhydride. The dispersion scale reading[11] (the so-called "z" reading) on the Zeiss Abbe refractometer for 1,3-pentadiene was 35.0, which is in the region of aromatic compounds (35) rather than aliphatic (41). The value for crotonaldehyde was found to be 36.1, but other conjugated unsaturated aliphatic compounds were higher: ethyl crotonate, 39.4; diketene, 41.0; methyl acrylate, 40.0.

Gas Analysis.—Two or three drops of liquid 1,3-pentadiene (prepared from 1-methylcrotoyl ether) and 75–100 cc. of air were drawn into a mercury-filled gas pipet. Complete vaporization was facilitated by adjusting the mercury level for diminished pressure within the pipet. Then the gas was transferred to the measuring buret of an Orsat type gas analysis apparatus equipped with a pipet containing maleic anhydride[12] at 100° and one containing 85% sulfuric acid. Five or six passes in the former (taking about forty-five minutes) were sufficient to absorb the pentadiene completely, and other unsaturated compounds if present were detected by absorption in sulfuric acid.

This analysis was recorded on the above sample of 1,3-pentadiene: sample, 100.0 cc.; after maleic anhydride, 80.5, 79.4, 79.2, 79.0, 79.0; after sulfuric acid, 79.0, 79.0. Hence there was complete absorption in maleic anhydride.

(1-Methylcrotyl)-trimethylammonium Hydroxide.—A mixture of 43 g. of (1-methylcrotyl)-trimethylammonium bromide, 57 g. of silver oxide and 60 g. of water was shaken overnight, then filtered. Since the filtrate foamed badly when boiled, it was added dropwise into a distilling flask heated by a bath at 150–160°. A coil condenser cooled by ice–salt and a trap containing dilute hydrochloric acid (to catch trimethylamine) were connected to the flask. The pyrolysis took eleven hours, and 17 ml. of a hydrocarbon layer was collected. The theoretical yield would have been 20 ml.

Distillation of this through a Podbielniak-type column, with some benzene added as a still base revealed a distillation plateau at 42–42.5° with no indication of a break at 49–51°, pointing to 1,3-pentadiene and the essential absence of 2,3-pentadiene.

Orsat analysis on 99.7, 99.4 and 99.9-cc. samples gave

---

[7] Cope and Overberger, THIS JOURNAL, **70**, 1433 (1948).

[8] Kuhn and Hoffer, *Ber.*, **63**, 2164 (1930); **64**, 1977 (1931).

[9] Delépine, *Ann. chim. phys.*, [5] **20**, 399 (1910); *Compt. rend.*, **150**, 535 (1910).

[10] Reif, *Ber.*, **39**, 1605 (1906); **41**, 2739 (1908).

[11] Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 3rd ed., 1948, p. 46.

[12] Tropsch and Mattox, *Ind. Eng. Chem., Anal. Ed.*, **6**, 104 (1934).

these buret readings after complete absorption in maleic anhydride: 76.2, 77.2, 71.8. The buret readings after absorption in 85% sulfuric acid were 75.0, 75.9, 70.2. These results pointed to the presence of 5.2, 5.5, 5.4% of *cis*-1,3-pentadiene in the sample which otherwise was *trans*.

(4-Chlorocrotyl)-trimethylammonium Chloride.—To 50 g. of 1,4-dichloro-2-butene, b. p. 157–159°, in 200 g. of dry dioxane was added 51 g. of liquid trimethylamine. Solid appeared at once. After two days it was collected and desiccated over sulfuric acid; yield, 67 g. Two crystallizations from absolute ethanol yielded 31 g. of pure white crystals, m. p. 174–176°.

Anal. Calcd. for $C_7H_{15}Cl_2N$: Cl, 38.6. Found: Cl, 37.2.

2-Butene-1,4-bis-(trimethylammonium Chloride).—Forty grams of trimethylamine was added to a solution of 35 g. of 1,4-dichloro-2-butene in 200 ml. of methanol. The solution turned dark red but no precipitate appeared. After three days the solvents were distilled off. Recrystallization of the desiccated solid from absolute alcohol was difficult, but a pure, white product (20 g.), m. p. 261° (dec.), was secured after four crystallizations.

Anal. Calcd. for $C_{10}H_{24}Cl_2N_2$: Cl, 29.2. Found: Cl, 28.9.

The same salt was formed if no solvent was employed, but trouble was encountered by caking. Also, the material was more difficult to decolorize and purify.

High Dilution Condensation of Crotonaldehyde.—The apparatus used was built according to the description of Adams and Kornblum.[13] Four grams of sodium was dissolved in 1500 ml. of methanol in the reaction flask. Fourteen grams of crotonaldehyde, dissolved in 500 ml. of methanol, was let into the flask through the dilution system during thirty-six hours (not continuous). The solvent was removed through an efficient column and the residue was made slightly acidic with acetic acid. Water was added, then ether. From the dried ($CaCl_2$) ether extract was obtained 0.5 g. of a sublimable solid. After recrystallization from benzene, it melted at 68.5–71.5°. Its odor, at first rather sweet, became rancid like that of butyric acid. Its water solution was acidic. It was soluble also in alcohol, ether, benzene. These properties fit those listed[9] for 2,6-dimethyl-5,6-dihydro-3-pyrancarboxylic acid.

Summary

Thermal degradation of (1-methylcrotyl)-trimethylammonium hydroxide gives rise to 1,3-pentadiene, chiefly the *trans* isomer. If 2,3-pentadiene was formed, it was in amounts too small to detect. This formation of conjugated double bonds is in contrast to the formation of both conjugated and cumulative double bonds in the degradation of 2,3-butanebis-(trimethylammonium hydroxide) and is in keeping with the results obtained by Willstätter in the synthesis of cycloöctatetraene.

Reactions of 1,4-dichloro-2-butene and trimethylamine are described. Experiments were performed on the condensation of crotonaldehyde and sodium methoxide at very high dilution in methanol.

EVANSTON, ILLINOIS

RECEIVED MAY 10, 1950

---

[13] Adams and Kornblum, THIS JOURNAL, **63**, 188 (1941).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY, LAFAYETTE, INDIANA]

Studies on the Synthesis of Lysine[1]

BY ED. F. DEGERING AND LESLIE G. BOATRIGHT

Lysine has been synthesized by a variety of methods. Several new methods have been published recently.[2,3,4] This report describes a new synthesis for lysine, preparation of some possible intermediates, and a reinvestigation of a portion of an earlier reported synthesis.[4]

$$\mathrm{HO{\cdot}(CH_2)_6{\cdot}OH\ (I) + HBr \rightarrow Br{\cdot}(CH_2)_6{\cdot}OH\ (II),\ then + HNO_3 \rightarrow Br{\cdot}(CH_2)_5{\cdot}CO_2H\ (III),\ then + Br_2 \rightarrow Br{\cdot}(CH_2)_4{\cdot}CHBr{\cdot}CO_2H\ (III),\ then + NH_3 \rightarrow H_2N{\cdot}(CH_2)_4{\cdot}CHNH_2{\cdot}CO_2H\ (V),\ then + HCl \rightarrow (H_3N\ (CH_2)_4{\cdot}CHNH_3{\cdot}CO_2H)^{++}\ 2Cl^-\ (VI)}$$

Compound II was prepared in yields of approximately 80% by use of an efficient liquid–liquid extractor to extract it from the reaction mixture as rapidly as it was formed. Petroleum ether was used as the extracting solvent and only small amounts of 1,6-hexanedibromide were obtained.

Oxidation of II was achieved by use of concentrated nitric acid as the oxidizing agent. Yields of 80% of III were obtained. Bromination of IV was accomplished according to the method of Merchant, *et al.*[5] Ammonolysis of IV with a large excess of aqueous ammonia followed by treatment with hydrochloric acid yielded DL-lysine dihydrochloride in 60% yield. A large excess of ammonia was necessary in order to prevent the formation of 2-piperidinecarboxylic acid by cyclization of IV. The over-all yield of DL-lysine dihydrochloride, based on the glycol I, was 38%.

Attempts were made to prepare open chain compounds from which lysine might be readily prepared, by cleavage of the ether linkage in certain furan derivatives. Ethyl 2-furylglycolate and 2-furylglycolic acid were prepared and subjected to high pressure hydrogenation in the presence of a copper chromite catalyst; however, no open chain compounds were isolated: C_4H_4O-CHO (furaldehyde, VII) + HCN→C_4H_4OCHOH-

---

[1] Abstracted from a thesis by Leslie G. Boatright, submitted to the Faculty of the Graduate School of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August, 1949. This work was sponsored by the National Institute of Health, through a fellowship grant to Mr. Boatright. Current addresses: Ed. F. Degering, Miner Laboratories, 9 S. Clinton, Chicago 6, Illinois, and Leslie G. Boatright, American Cyanamid Company, Stamford, Connecticut.

[2] Gaudry, *Can. J. Research*, **B26**, 387 (1948).

[3] Rogers, *et al.*, THIS JOURNAL, **71**, 1837 (1949); Warner and Moe, *ibid.*, **70**, 3918 (1948).

[4] Sayles and Degering, *ibid.*, **73**, 3161 (1949).

[5] Merchant, Wickert and Marvel, *ibid.*, **49**, 1828 (1927).