melting at 183°. Evidently heating the substance with benzyl alcohol caused decomposition. Subsequent crystallization from the same solvent gave finally a perfectly white product, melting at 194°. This white substance is the diacetate of *o*-hydroxy-oxanilide, identified by analysis and a mixed melting point with a synthetic sample prepared by the method of Meyer and Seeliger.[4] These investigators give 201° as the melting point of the diacetate. This melting point is too high; a purified sample melted at 194° (corr.).

Anal. Subs., 0.2002, 0.1891: CO_2, 0.4461, 0.4203; H_2O, 0.0816, 0.0796. Calcd. for $C_{18}H_{16}O_6N_2$: C, 60.67; H, 4.50. Found: C, 60.77, 60.61; H, 4.52, 4.73.

The red acetate may be decomposed by dissolving in benzyl alcohol and heating for a few minutes. The solution is completely decolorized.

Summary

A new condensation product of *o*-aminophenol and oxalic acid has been isolated and some derivatives of it are described.

PULLMAN, WASHINGTON

TRIMETHYLACETALDEHYDE AND DIMETHYLETHYLACETALDEHYDE

BY J. B. CONANT, C. N. WEBB AND W. C. MENDUM

Now that tertiary butyl and tertiary amyl alcohols are available, it becomes possible to prepare trimethylacetaldehyde and dimethylethylacetaldehyde in quantities suitable for synthetic work. These aldehydes promised to be of interest in connection with the study of highly-branched compounds which is being carried on in the Harvard Laboratories. In this paper we shall describe the preparation and behavior of these aldehydes in certain reactions. Although the hope of using these substances as a starting point in the synthesis of other branched compounds now seems dim, the results which have come to light are of some general interest.

The procedure we employed in the preparation of both aldehydes is outlined below

$$R_3COH \xrightarrow{HCl} R_3CCl \longrightarrow R_3CMgCl \xrightarrow{HCHO} R_3CCH_2OH \longrightarrow R_3CCHO + H_2$$
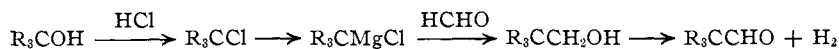
The last step, the dehydrogenation, is the same as that employed by Franke[1] in the most recent synthesis of trimethylacetaldehyde. We followed Bouveault's procedure instead of Franke's, however, and using copper at 250–300° obtained a 64–66% yield of aldehyde from both primary alcohols. The yield from the tertiary alcohol to the primary alcohol in both series was 40–50%, making the over-all yield for the four steps given above 25–33%.

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[4] Meyer and Seeliger, *Ber.*, **29**, 2644 (1896).

[1] Franke and Hinterberger, *Monatsh.*, **43**, 657 (1922).

One rather unexpected result was encountered in the preparation of the primary alcohols. If a considerable excess of gaseous formaldehyde is passed into the Grignard reagent, the reaction mixture decomposed and the product isolated in the usual way, as much as two-thirds of the product may be the acetal, $H_2C(OCR_3)_2$. The acetals are high-boiling liquids from which the tertiary alcohols may be obtained by heating with alcoholic hydrochloric acid. Although they are not appreciably decomposed by distillation with steam from 30% sulfuric acid, they appear to be decomposed to some extent by steam distillation of the reaction mixture. This procedure, together with a careful control of the amount of formaldehyde, results in relatively little high-boiling material and the maximum yield of carbinol. An alternative scheme is to employ an excess of formaldehyde and then boil the entire crude product with alcoholic hydrochloric acid, thus regenerating the carbinol from the acetal.

Dimethylethylacetaldehyde was prepared by Faworski[2] with very poor yields by chromic acid oxidation of the primary alcohol. Our product yielded a semicarbazone with the same melting point as that reported.

Autoxidation and Photochemical Decomposition.—Both trimethylacetaldehyde and dimethylethylacetaldehyde rapidly undergo autoxidation in the air. Samec[3] has shown that the final product in the first case is trimethylacetic acid and we have obtained as much as 82% of dimethylethylacetic acid by the autoxidation of the corresponding aldehyde. The phenomenon of the autoxidation of both these aliphatic aldehydes seems to be very similar to the autoxidation of benzaldehyde. After a short exposure to air, peroxide is present, as shown by the liberation of iodine from acidified potassium iodide solution. If a sample of aldehyde containing the peroxide is allowed to stand out of contact with air, the peroxide disappears, presumably because it is used up in the oxidation of a further amount of the aldehyde to acid. The autoxidation is retarded by the presence of hydroquinone. This was determined by following the process of oxidation by the titration of the acid formed; it was also found that the peroxide developed much more slowly. Although the rate of oxidation of pure trimethylacetaldehyde is of the same order of magnitude as that of pure benzaldehyde, the effect of the hydroquinone is much greater on the aromatic substance.

It was noticed early in our work that the liquid aldehyde slowly evolved gas and the evolution proceeded more rapidly in diffused daylight than in the dark. As much as 30 cc. of gas was evolved from 40 g. of aldehyde in the course of a day. The gas was found to be carbon monoxide. The

[2] Faworski, *J. Russ. Phys.-Chem. Soc.*, **50**, 43 (1918), *Chem. Zentr.*, III, 667 (1923); Bouveault, *Bull. soc. chim.*, [3] **31**, 1326 (1904), obtained the compound in traces and analyzed the semicarbazone.

[3] Samec, *Ann.*, **351**, 259 (1907).

decomposition of aliphatic aldehydes by the action of ultraviolet light according to the equation RCHO $\longrightarrow$ RH + CO has been studied by Franke and Pollitzer.[4] The action of ultraviolet light on trimethyl-acetaldehyde was shown by Hinterberger[5] to cause the evolution of carbon monoxide, presumably as a result of the same reaction. We have been able to show that this is, indeed, the case since we isolated *iso*butane from a sample of pure trimethylacetaldehyde which was allowed to decompose for many weeks in daylight in the absence of oxygen.

A few preliminary experiments were performed to outline in a general way the photochemical behavior of these trisubstituted aldehydes. About 40 g. of aldehyde was employed and the rate of gas evolution per hour measured when illuminated by a quartz mercury arc lamp. The rate of decomposition was about the same in both quartz and pyrex flasks but was reduced to one-half by the interpolation of 1.45 mm. of soft glass and to about 20% by 1 mm. of mica. These facts enabled us to estimate the range of effective light from an inspection of photographs of the iron arc which were taken through our pyrex flask, glass plate and mica sheet. We are indebted to Mr. W. C. Root for these spectrograms. The limits of transmission were: pyrex, 2950 Å.; mica, 3020 Å. (3020 to 3150 Å. weak); glass, 3100 Å. (3100 to 3150 Å. weak). Since pyrex and quartz were photochemically equivalent in our reaction, whereas both mica and glass greatly diminished the effectiveness of the light, we conclude that it is primarily light of a wave length of 2950 to 3200 Å. that is responsible for the photochemical decomposition of trimethylacetaldehyde.

It is a well-known fact that the autoxidation of benzaldehyde is accelerated by ultraviolet light and we found a two-fold increase in the autoxidation of trimethylacetaldehyde when it was exposed to a quartz mercury arc. It is an interesting question for further research to decide what connection, if any, exists between the autoxidation reaction and the decomposition into carbon monoxide. That there is some connection is suggested by the facts just mentioned and also by our observation that the addition of 1 part in 500 of hydroquinone decreases to a third the photochemical decomposition in ultraviolet light.

Cannizzaro Reaction.—Although the Cannizzaro reaction is often supposed to be a general reaction of aldehydes which have no hydrogen in the α-position, Hinterberger[5] could obtain no evidence of this reaction with trimethylacetaldehyde. He used a concentrated solution of potassium hydroxide in water and some alcohol. Using 50% alcoholic potassium hydroxide containing a little water we obtained, after letting the homogeneous solution stand for one day at room temperature, a 59% yield of the carbinol and 55% yield of the acid. The Cannizzaro reaction

[4] Franke and Pollitzer, *Monatsh.*, **34**, 797 (1913).

[5] Hinterberger, "Dissertation," Vienna, **1923**.

thus does proceed with this aldehyde to at least 60% if alcohol is used as a mutual solvent for the alkali and the aldehyde. When we used aqueous alkali, however, we obtained chiefly unchanged aldehyde and indefinite higher boiling condensation products.

The Action of the Grignard Reagent.—The usual addition reaction between the Grignard reagent and an aldehyde is complicated in the case of aldehydes of the type R_3CCHO by the appearance of a reduction reaction which leads to the carbinols R_3CCH_2OH. Which of these two competing reactions predominates is determined by the nature of the hydrocarbon residue attached to the magnesium atom of the Grignard reagent. Thus with n-propylmagnesium bromide and dimethylethyl-acetaldehyde 15% reduction was observed, with *iso*propylmagnesium bromide 33% and with *tert.*-butylmagnesium chloride the reduction was 65%; in this last case there was no evidence of an addition reaction. With trimethylacetaldehyde, the process of reduction is slightly less pronounced than with its homolog; thus with the n-propyl Grignard reagent there was only a trace of reduction as compared with 15% with dimethylethylacetaldehyde, and the yield of addition product was 50% against 45%. With *iso*propylmagnesium bromide the figures were: trimethylacetaldehyde, reduction 10%, addition 33%; dimethyl-ethylacetaldehyde, reduction 33%, addition 27%. The distinction between the two aldehydes thus seems to be just sufficient to be detected by our methods. Similar results have been obtained in this Laboratory in a study of the action of the Grignard reagent on ketones[6] and it is not necessary in this paper to discuss again this interesting effect of branching the chain in carbonyl compounds and Grignard reagents.

Experimental

(A) **Preparation of Trimethylacetaldehyde.**—*Tert.*-butylcarbinol was prepared from *tert.*-butylmagnesium chloride[7] and formaldehyde by a modified Courtot procedure.[8] The directions for the preparation of cyclohexylcarbinol by this procedure are given in detail in a recent volume of "Organic Syntheses"[9] and need only be briefly referred to here. Three moles of Grignard reagent was prepared and the passing in of the formal-dehyde vapor required five to six hours. Some difficulty was encountered by the clogging of the entrance tube with solid paraformaldehyde. This was overcome by using a T-tube and running a rod down from time to time. The reaction mixture was hydrolyzed with dilute sulfuric acid, steam distilled and the carbinol purified by frac-tionation through a long column. The yield was 42 to 50% of the theoretical based on the magnesium. The product boiled at 112–114° and melted at 47–49°.

Di-*tert.*-butyl Acetal of Formaldehyde, $H_2C(OC(CH_3)_3)_2$.—Small amounts of this substance were obtained as a high-boiling fraction in the *tert.*-butylcarbinol prepared as described above. In one experiment in which 4.2 moles of formaldehyde vapor

[6] Conant and Blatt, THIS JOURNAL, **51**, 1227 (1929).

[7] "Organic Syntheses," John Wiley and Sons, Inc., New York, **8**, 40 (1928).

[8] Courtot, *Bull. soc. chim.*, [3] **35**, 985 (1906).

[9] "Organic Syntheses," John Wiley and Sons, Inc., New York, **6**, 22 (1926).

was introduced into the reagent formed from 3 moles of magnesium, the yield of acetal was 40 g. (0.25 of a mole). The acetal distils at 182–185°. It was not affected by steam distillation from 80% sulfuric acid but was converted into *tert.*-butylcarbinol by heating with an equal weight of 95% ethyl alcohol containing 2 cc. of concd. hydrochloric acid.

Anal. Calcd. for $C_9H_{20}O_2$: C, 70.2; H, 12.8. Found: C, 70.3, 70.0; H, 12.4, 12.5.

Dehydrogenation of the Carbinol.—The method of Bouveault[10] was followed. A copper catalyst was placed in a vertical pyrex tube 2 cm. in diameter and 80 cm. long. This was attached directly to the flask containing the carbinol, the contents of which were kept boiling by means of a Bunsen burner. The tube containing the catalyst was heated electrically to a temperature of 250–300°. The vapors after passing from the flask up through the catalyst were fractionated by means of a long spiral column and the higher-boiling portion returned to the flask by means of a tube leading back from the bottom of the fractionating column. By controlling the rate of distillation with reference to the temperature at the top of the column it was possible to obtain a distillate consisting very largely of the aldehyde. On redistillation through a column, aldehyde boiling at 74–76° was obtained in a yield of 60–66%. The copper catalyst prepared according to Bouveault's directions was found satisfactory for the preparation of both trimethylacetaldehyde and dimethylethylacetaldehyde and was used in a number of runs. The catalyst is subject to poisoning rather easily, however, and in subsequent work many attempts to prepare an active catalyst failed for no apparent reason.

(B) **Preparation of Dimethylethylacetaldehyde.**—The *tert.*-amylcarbinol, $(CH_3)_2$-$C(C_2H_5)CH_2OH$, was prepared from *tert.*-amylmagnesium chloride and formaldehyde exactly in the same manner as the *tert.*-butylcarbinol. In preparing the Grignard reagent from *tert.*-amyl chloride it was noticed that if the amount of ether was insufficient a precipitate formed and the mixture became very thick. The following directions were satisfactory for the preparation of 3 moles of reagent. A 3-liter 3-necked flask was fitted with a stirrer, condenser and dropping funnel. Seventy-two g. of magnesium and a little iodine were placed in the flask. About 150 cc. of ether was added, then 30–40 cc. of chloride, with stirring. In a short time a vigorous reaction started, the flask was cooled and about 500 cc. of ether added as fast as possible. When the reaction slowed down the remainders of 1500–1600 cc. of ether and 360 g. of chloride were mixed and added slowly at such a rate that the mixture boiled gently; this required about six hours. The *tert.*-amylcarbinol boiling at 135–138° (Bouveault and Blanc[11] give 135°) was obtained in yields of 40–47%.

Di-*tert.*-amyl Acetal of Formaldehyde, $H_2C(OC_5H_{11}-tert.)_2$.—This acetal was obtained as a by-product from the preparation of the *tert.*-amylcarbinol. In one run a large excess of formaldehyde was used and the acetal was the principal product (the reaction mixture was not steam-distilled). The acetal distils at 220–224°. On boiling an alcoholic solution of it containing a little concd. hydrochloric acid it is converted into the *tert.*-amylcarbinol; 5 g. yielded 4 g. of carbinol and the presence of an aldehyde in the solution was shown by Schiff's reagent. The compound does not react with any of the following reagents: methylmagnesium iodide in amyl ether, alcoholic potassium hydroxide, phenyl isocyanate, *p*-nitrophenylhydrazine.

Anal. Calcd. for $C_{11}H_{24}O_2$: C, 72.2; H, 13.0. Found: C, 71.9, 71.6; H, 12.8; 13.0. *Mol. wt.* by freezing-point method in benzene: calcd. for $C_{11}H_{24}O_2$: 216. Found: 208, 213.

10 Bouveault, *Bull. soc. chim.*, [4] **3**, 119 (1908).

11 Bouveault and Blanc, *ibid.*, [3] **31**, 749 (1904).

Dimethylethylacetaldehyde, $(CH_3)_2C(C_2H_5)CHO$.—The dehydrogenation of the *tert.*-amylcarbinol was carried out in the apparatus described above. The yield of aldehyde which boiled at 101–107° was 60–66%. The boiling point of the pure aldehyde is 104 ± 0.5°; this value was obtained both with a carefully refractionated material and with aldehyde regenerated from the bisulfite compound. The semihydrocarbazone melted at 153–155°, as reported by Faworski and by Bouveault.[2] A crystalline bisulfite compound was formed by shaking the aldehyde with an aqueous saturated solution of sodium bisulfite also saturated with sulfur dioxide. The aldehyde was regenerated by the action of sodium carbonate solution. The bisulfite compound is oxidized by air rather rapidly.

Anal. Calcd. for $C_6H_{12}O$: C, 72.0; H, 12.0. Found: C, 71.1, 71.2; H, 12.1, 12.2. *Refractive Index.* $n_D^{22°} = 1.3975$; $d_4^{22} = 0.8040$; M_D (n^2 formula) = 29.99. Calcd., 29.92.

(C) **Autoxidation.**—It is known that the product of autoxidation of trimethylacetaldehyde is trimethylacetic acid. To prove that the dimethylethylacetaldehyde forms the corresponding acid the following experiment was made: Five g. of the aldehyde was placed in a 500-cc. flask fitted with a stopcock and full of oxygen. The flask was attached to a manometer. The stopcock was opened from time to time and the pressure read. It was noticed that the pressure in the flask fell considerably during the early part of the reaction. The flask was allowed to stand for twenty-nine days and then the material was removed. The acid content was determined by means of excess standard base and standard acid. It was found to be 82.1% acid by weight. The acid was then distilled. The major portion distilled between 180–188°, the boiling point of the acid being 186°.

The rate of oxidation of trimethylacetaldehyde to acid both in air and oxygen, with and without hydroquinone, was determined. One gram of the aldehyde was placed in a 300-cc. flask containing air or oxygen and from time to time a sample was removed and its acid content determined by dissolving in excess standard base and titrating back with standard acid, using phenolphthalein as an indicator. The inaccuracy of this method is probably in the neighborhood of 1%. The end-point in the case of the samples containing hydroquinone was rather uncertain. The amount of hydroquinone used in the protected samples was about 1 part in 500. The aldehyde employed contained only a trace of acid. Some typical results showing the percentage of oxidation at different times are as follows: (1) trimethylacetaldehyde in oxygen: 1.75 hrs., 44%; 5.75 hrs., 67%; 18.7 hrs., 83%; 24.9 hrs., 88%; 44.2 hrs., 87%—(2) trimethylacetaldehyde containing 1 part in 500 of $C_6H_4(OH)_2$ in oxygen: 1.75 hrs., 9%; 5.75 hrs., 22%; 18.7 hrs., 57%; 25 hrs., 65%; 43.5 hrs., 73%; 48.75 hrs., 74%—(3) trimethylacetaldehyde in air: 7.75 hrs., 43%; 25 hrs., 60%; 32.25 hrs., 77%—(4) trimethylacetaldehyde with 1 part in 500 of $C_6H_4(OH)_2$ in air: 5 hrs., 3%; 20.75 hrs., 11%.

(D) **Photochemical Decomposition of the Aldehydes.**—When either of the aldehydes was sealed into a flask containing air connected to a manometer it was noticed that the pressure first fell off and then increased. The increase in pressure continued a long time, being continuously observed for over a month. This increase was not noticed when the flask was covered with black paper. The only logical explanation was that either the aldehyde or some oxidation product was being decomposed by light to a gaseous product. To decide this question about 40 g. of aldehyde was placed in a small flask which was connected to a gas buret

filled with mercury. The leveling bulb was kept a little above the mercury level in the buret in order to keep a slight pressure on the system and to prevent leaks inward. After the apparatus had stood for a day or so, it was noted that gas came off, the rate of evolution seemingly increasing with time up to a more or less definite maximum. The amount seemed to be greater the brighter the day. It was noted that the gas was evolved whether the gas above it were air or nitrogen and whether or not the aldehyde had peroxide in it. In the case both of trimethyl- and dimethylethylacetaldehyde, amounts of gas as great as 30 cc. were given off in a day from 40 g., although the amount given off was generally much less than this. It was also noted that if the flask were covered with black paper, the evolution of gas stopped. It was also found that addition of hydroquinone stopped the formation of gas. The gas obtained was analyzed from time to time using the regular methods of gas analysis. The gas both from dimethylethylacetaldehyde and trimethylacetaldehyde had about the same composition. A typical analysis is as follows: CO_2, 0.9%; O_2, 1.0%; CO, 76.1%; material soluble in fuming sulfuric acid, 13.1%; residue incombustible, 8.8%.

A sample of 30 g. of aldehyde which had been giving off gas to a closed system for several weeks (the evolution being most rapid on bright days) was connected to a gas buret through a return condenser and boiled under diminished pressure. About 345 cc. of gas was thus obtained (some air was introduced in connecting the apparatus); of this 7 cc. only dissolved in concd. sulfuric acid. Of the remainder, 25 cc. condensed to a liquid at $-40°$. This liquid on evaporation yielded a gas which was identified as *iso*butane by its liquefaction point, $-9°$ to $-14°$, and its failure to react with concd. sulfuric acid or bromine water.

The action of ultraviolet light was studied using a Cooper-Hewitt Lab. Arc 105–125 V, 1 Amp., Type K 210,230. The results could not be exactly duplicated because the conditions and the output of the lamp could not be accurately controlled. It was found that if 38 g. of aldehyde in a pyrex flask was exposed to the rays from the arc located about 3 inches away, the gas evolved in the first hour (the aldehyde being taken from the dark) was approximately 20 cc., or of the order of the amount of gas given off in a day in good sunlight. The rate of evolution greatly increased during the time of exposure and after the light was turned off gas came off for the next half hour at a high rate. If the aldehyde was placed in quartz the amount of gas in the first hour was about 25 cc. The placing of one glass plate of 1.45 mm. thickness in front of the flask cut the amount of gas down to about 14 cc.; more glass plates had little effect. Passing the rays through 0.9 mm. of mica cut the rate down to 5 cc. in the first forty minutes; the use of only 0.17 mm. of mica gave almost the same result. The addition of hydroquinone in the proportion

of 1 in 500 decreased the evolution of gas to approximately 8 cc. in the first hour.

(E) **The Action of the Grignard Reagent.**—The general procedure was to prepare the Grignard reagent from magnesium and the alkyl chloride or bromide in the usual way. Usually 0.4 of a mole of alkyl halide in a total of 225 cc. of ether was used. The aldehyde containing a trace of hydroquinone diluted with 4 to 6 times its volume of ether was run into the well-stirred solution of the Grignard reagent kept at 0°. The reaction mixture after standing overnight at room temperature was warmed to the boiling point of ether for about one hour and then decomposed in the usual way with ice-cold dilute sulfuric acid. With those reagents which caused reduction there was a vigorous evolution of gas when the reaction mixture was warmed; this gas was in part unsaturated hydrocarbons, since it decolorized bromine water. The crude product from the decomposition of the reaction mixture was separated as far as possible by fractional distillation through a spiral column of the Widmer type. The presence or absence of carbinols in the fractions was determined by adding phenyl isocyanate and obtaining the crystalline phenylurethans where possible.

The results are summarized below; unless otherwise stated the Grignard reagent in each case was prepared from 0.41 g. atom of magnesium and a slight excess of alkyl halide. There was thus a large excess of reagent in every case.

Trimethylacetaldehyde and *n*-Propylmagnesium Bromide.—0.12 Mole of aldehyde yielded 0.06 mole of $(CH_3)_3CCHOHCH_2CH_2CH_3$, b. p. 151–157°; phenylurethan, m. p. 69–71°.[12] The fraction at 120–151° was only 1 g. and gave a slight amount of the phenylurethan of $(CH_3)_3COH$.

Trimethylacetaldehyde and *Iso*propylmagnesium Chloride.—0.12 Mole of aldehyde yielded 0.04 mole of $(CH_3)_2CCHOHCH(CH_3)_2$, b. p. 140–150°, phenylurethan 87–88°.[13] The fraction at 110–125° gave the phenylurethan of $(CH_3)_3CCH_2OH$; a slight intermediate fraction at 125–140° yielded what seemed to be a mixture of the two phenylurethans. Neglecting the primary alcohol in this fraction the amount of reduction product was 0.01 mole.

Trimethylacetaldehyde and *Tert.*-butylmagnesium Chloride.—0.3 of a mole of Grignard reagent (by analysis) in 180 cc. of clear ethereal solution and 0.2 mole of aldehyde yielded 0.13 mole of $(CH_3)_3CCH_2OH$, b. p. 110–111°, which solidified. No other product could be found.

Dimethylethylacetaldehyde and *n*-Propylmagnesium Bromide.—0.10 Mole of aldehyde gave 0.015 mole of *tert.*-amylcarbinol, b. p. 130–140°, yielding the known phenylurethan, and 0.045 mole of $(CH_3)_2C(C_2H_5)CHOHCH_2CH_2CH$, b. p. 175–180°, 3,5-dinitrobenzoyl ester (from the chloride and pyridine), m. p. 70–71°. There was

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[12] Haller and Bauer, *Ann. chim. phys.*, [8] **29**, 317 (1913). We also synthesized the carbinol in 47% yield from *n*-butylaldehyde and *tert.*-butylmagnesium chloride.

[13] Haller and Bauer, ref. 12, give the melting point of the urethan as 79°, but this is probably a misprint for 89°, since this is the melting point of a pure sample prepared from the carbinol synthesized from *tert.*-butylmagnesium chloride and *iso*butyraldehyde.

a slight intermediate fraction. Since the carbinol was unknown it was also synthesized by the action of *tert.*-amylmagnesium chloride on *n*-butyraldehyde; the yield was only 25%. The pure carbinol boils at 177–178° and the phenylurethan is obtained with difficulty. The 3,5-dinitrobenzoyl ester is more useful for identification; it melts at 71.5–72.5°.

Analysis of Tert.-amyl n-Propylcarbinol.—Calcd. for $C_9H_{20}O$: C, 75.0; H, 13.9. Found: C, 75.5; H, 13.9.

Dimethylethylacetaldehyde and *Iso*propylmagnesium Bromide.—0.09 Mole of aldehyde yielded 0.030 mole of *tert.*-amylcarbinol, b. p. 133–134°, a small intermediate fraction, and 0.024 mole of *tert.*-amyl-*iso*propylcarbinol, b. p. 167–177° (Haller and Bauer give the b. p. as 170–171°; we were unable to obtain a pure crystalline phenylurethan from our product).

Dimethylethylacetaldehyde and *Tert.*-butylmagnesium Chloride.—0.05 Mole of aldehyde added to the reagent from 0.11 mole of magnesium yielded 0.03 mole of *tert.*-amylcarbinol, b. p. 130–137°; the higher and lower boiling fractions were very slight.

(F) **Cannizzaro Reaction.**—Ten g. of trimethylacetaldehyde was stirred with 15 cc. of 95% alcohol, 2 cc. of water and 7 g. of potassium hydroxide (the solution was cooled before the aldehyde was added) for a day. The mixture was homogeneous. The mixture was poured into water and ether extracted; the extract was dried and distilled through a short column. A strong smell of aldehyde was noticed in the ether distillates. The fractions collected were: 110–116°, 2.5 g.; 116–120°, 0.5 g.; residue 0.5 g. Both the 110–116° and the 116–120° fractions became solid in less than ten minutes on treatment with phenyl isocyanate, forming the phenylurethan of *tert.*-butylcarbinol. The potassium hydroxide solution was acidified and extracted with ether. The extract was dried and distilled: 155–163° (most at 159–164°), 3.3 g. or 55%; residue, 0.5 g.

Three attempts to carry out the Cannizzaro reaction with aqueous sodium hydroxide failed. An emulsion of the aldehyde in 50% aqueous sodium hydroxide for a day at room temperature yielded only a trace of *tert.*-butylcarbinol though a small amount of acid was formed. The chief neutral product boiled over a very wide range. Use of 30% sodium hydroxide, while keeping the emulsion stirred for two and one-half days, gave no evidence of carbinol formation and only a trace of acid which might have come from atmospheric oxidation. Evidently in all three cases large amounts of aldehyde remained unchanged and were contaminated with a mixture of higher boiling neutral substances.

Summary

1. A procedure is described for the synthesis of trimethylacetaldehyde and dimethylethylacetaldehyde from *tert.*-butyl and *tert.*-amyl alcohols.

2. Both aldehydes undergo autoxidation in the air. The process is retarded by the presence of traces of hydroquinone.

3. Both aldehydes undergo photochemical decomposition in bright daylight and in light from a mercury lamp. The effective wave lengths appear to be 2950–3200 Å. The products of the reaction are carbon monoxide and the saturated hydrocarbon.

4. The Cannizzaro reaction may be carried out with trimethylacetaldehyde if alcoholic potassium hydroxide is employed.

5. The action of the Grignard reagent from *n*-propyl, *iso*propyl and *tert.*-butyl halides on the two aldehydes has been studied. The reagent

from the primary and secondary halides gives addition and reduction products; with the *tert.*-butylmagnesium chloride only reduction occurred.

CAMBRIDGE, MASSACHUSETTS

THE ISOELECTRIC POINT OF CRYSTALLINE UREASE[1]

BY JAMES B. SUMNER AND DAVID B. HAND

Introduction

In connection with our study of the properties of crystalline urease[1a] we have been especially interested in finding the isoelectric point inasmuch as it has never been determined for an isolated enzyme. We thought that a knowledge of this value would help to classify urease among proteins, would aid in improving the method of purification and might eventually throw light on the mode of action of the enzyme on urea.

References to the isoelectric points of enzymes are not lacking in the literature and some of these references are contradictory. Some enzymes have been stated to function as ions over the P_H range at which they are active; other enzymes have been found to have isoelectric points coinciding with the P_H of their optimum activity and consequently they are thought to react best when not ionized. Thus, pepsin was found by Michaelis and Davidsohn[2] to have an isoelectric point at P_H 2.26. These authors state that pepsin must be positively charged to have a proteolytic effect. Northrop,[3] however, from a study of the distribution of pepsin and chloride and bromide ions between solid gelatin or coagulated egg albumin, concludes that pepsin is a monovalent ion from P_H 1 to 7. Michaelis[4] states that with invertase the uncharged particles are active, that with trypsin, erepsin, lipase and maltase the anions are the active part, while with pepsin the cation is active. Michaelis and Pechstein[5] have found the isoelectric point of liver catalase to be at P_H 5.37 and believe that the anions and uncharged particles are active, while the cations are not. Northrop[6] thinks it probable that the isoelec-

[1a] J. B. Sumner, *J. Biol. Chem.*, **69**, 435 (1926); **70**, 97 (1926); J. B. Sumner and D. B. Hand, *ibid.*, **76**, 149 (1928); *Naturwissenschaften*, **16**, 9, 145 (1928); J. B. Sumner and R. G. Holloway, *J. Biol. Chem.*, **79**, 489 (1928).

[2] L. Michaelis and H. Davidsohn, *Biochem. Z.*, **28**, 1 (1910).

[3] J. H. Northrop, *J. Gen. Physiol.*, **7**, 603 (1924–1925).

[4] L. Michaelis, *Biochem. Z.*, **60**, 91 (1914).

[5] L. Michaelis and H. Pechstein, *ibid.*, **53**, 320 (1913).

[6] J. H. Northrop, *J. Gen. Physiol.*, **6**, 337 (1923–1924).