

metry, thus indicating comparative freedom from interaction, and for resolution. The results of these analyses are given in Table II. In these computations allowance for the  $\delta$  and  $\epsilon$  effects has been made by assuming that the latter are additive and are equal to the effects observed in solutions of the purified constituents at the same pH, ionic strength, and protein concentration as that of the corresponding component in egg white. While we have made no systematic study of the composition of egg white, we have observed some variation of material from different sources. Thus the percentage of ovalbumin has varied from 60 to 70% while the conalbumin has varied from 13 to 18%. The table also gives the results obtained by Sørensen<sup>27</sup> for the composition of egg white, using chemical methods.

### Summary

Electrophoretic patterns of egg white have been obtained over a range of pH values. These patterns have indicated seven electrically distinguishable components: *viz.*, ovalbumin, A<sub>1</sub> and A<sub>2</sub>, ovomucoid, O, conalbumin, C<sub>1</sub>, and three globulins, G<sub>1</sub>, G<sub>2</sub> and G<sub>3</sub>. The identity of these components has been established by comparison with patterns obtained from the purified components,

(27) M. Sørensen, *Compt. rend. trav. lab. Carlsberg*, **20**, no. 3 (1933-1935).

with the exception of the globulins which have not yet been separated.

Each step in a separation of ovalbumin has been followed electrophoretically, indicating in this process the relatively greater efficiency of crystallization over salting out. Ovalbumin has been shown to consist of two components both in egg white and in the purified state.

The separation of conalbumin involves a modification into a form, C<sub>2</sub>, which slowly reverts, above pH 4, to the normal form, C<sub>1</sub>, in which it exists in egg white.

Ovomucoid, though not electrically separable into more than one component, shows complexity as indicated by "reversible boundary spreading."

The mobilities of the components have been determined over the range of pH 3.9 to 8, which includes isoelectric points of all constituents except the globulin G<sub>1</sub>.

Evidence is given of protein-protein complexes, especially when the components carry opposite electrical charges. The extent of this association increases with protein concentration and decreasing ionic strength.

An analysis of egg white has been obtained electrophoretically.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

## *alpha*-Bromo Secondary Alkyl Ketones. I. Reaction with Sodium Alcoholates. A New Synthesis of Tertiary Acids by Rearrangement<sup>1,2</sup>

BY J. G. ASTON AND R. B. GREENBURG

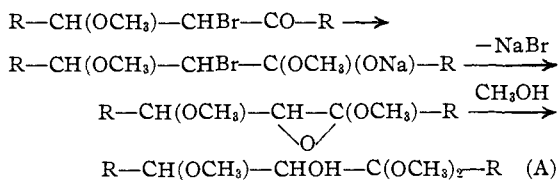
The problem of replacement of  $\alpha$ -halogen in ketones by bases has been considered in detail by Kohler and co-workers.<sup>3a,b</sup> Kohler and Addinall<sup>3a</sup> called attention to the fact that in the synthesis of  $\beta$ -diketones by the action of alcoholates on  $\alpha,\beta$ -dibromo ketones a second reaction can occur, namely, one producing  $\beta$ -alkoxy- $\alpha$ -hydroxy acetals. They formulated the reaction as occurring through the  $\alpha$ -bromo- $\beta$ -alkoxy ketone (which is supposed to be an intermediate in the production of the  $\beta$ -diketone) as follows

(1) From the doctorate thesis of R. B. Greenburg, The Pennsylvania State College, 1940.

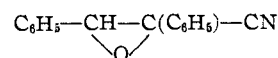
(2) Certain preliminary reactions were carried out several years ago by W. D. Moyer and R. R. Heterick.

(3) (a) Kohler and Addinall, *THIS JOURNAL*, **52**, 3728 (1930);

(b) Kohler and Brown, *ibid.*, **55**, 4299 (1933).

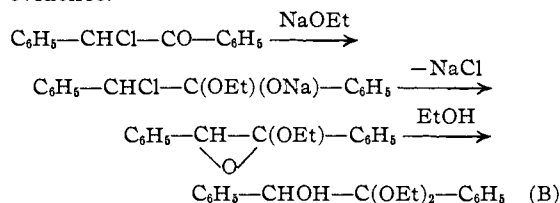


This second reaction gave a clue to the reaction involved in the synthesis of the  $\beta$ -diketones. The precedent for the last step was supplied by Kohler and Brown,<sup>3b</sup> who studied the reaction of potassium cyanide on desyl chloride and thus obtained two stereoisomeric oxido-nitriles



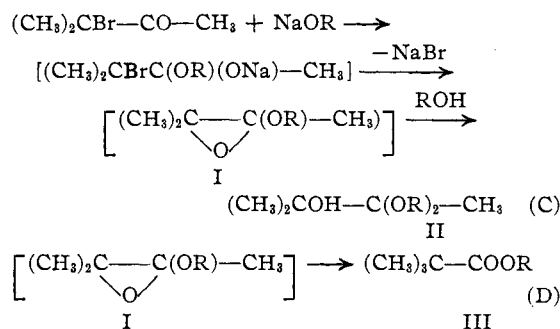
However, desyl chloride had already been shown

by Ward<sup>4</sup> to react with sodium ethylate to produce the ethyl acetal of benzoin, which Ward postulated as follows without any experimental evidence.



The experimental work in the present paper shows that this simple and seemingly general reaction is accompanied by a rearrangement of the postulated intermediate ethylene oxide which gives rise to quite a different product, namely, the trialkyl-acetic ester. The formation of this ester is in itself a strong indication of the validity of the mechanism originally formulated by Ward and needs no reference to analogous reactions.

It will be simplest first to consider what happens when 3-bromo-3-methyl-2-butanone is treated with sodium ethylate in absolute ethanol. Two reactions occur



The 3,3-diethoxy-2-methyl-2-butanol (II, R = Et) is the expected product and is formed to the extent of 32%. With semicarbazide hydrochloride and sodium acetate in water no semicarbazone is formed except after long standing, whereas if first treated with cold dilute acid 3-hydroxy-3-methyl-2-butanone semicarbazone is formed at once. Similarly the 2,4-dinitrophenylhydrazones can be formed and this was the basis of identification. The methyl trimethylacetate (III) formed 13.5% of the reaction products.

When sodium isopropylate is used in isopropyl alcohol, isopropyl trimethylacetate is formed in 20% yield and the corresponding hydroxy-acetal in only 8% yield. The low yields are undoubtedly due to the difficulty of separating the products from the relatively large amount of solvent

alcohol. This result is rendered entirely reasonable by the ratio of products formed with sodium methylate. In this case 76.5% of the hydroxy-acetal can be isolated but it was not possible to detect any ester.

In order to obtain methyl trimethylacetate by the action of sodium methylate it is necessary to employ an ether suspension of the latter. The reaction proceeds smoothly according to (D) at room temperature, forming 39% of methyl trimethylacetate and 12% of the hydroxy-acetal. The latter was, no doubt, due to the excess methyl alcohol used in preparing the sodium methylate (50% in excess of the amount necessary). Correspondingly, ethyl trimethylacetate can be obtained as the sole product of reaction of sodium ethylate if an ether suspension of sodium ethylate is used. When there was no excess ethyl alcohol, 61.3% of ethyl trimethylacetate was obtained. Isopropyl trimethylacetate was obtained in 64% yield under similar circumstances when an ether suspension of sodium isopropylate was used without any excess of the alcohol present.

When there is no alcohol present, the last step in reaction (C), which requires the alcohol, is not possible. That reaction (D) can occur at room temperature (or at any temperature) is not *a priori* obvious but nevertheless seems to be a fact. This mode of cleavage of an ethylene oxide ring may be associated with the small amount of steric hindrance. At any rate the formation of the ester is quite general, for when 2-bromo-2-methyl-3-pentanone is treated with an ether suspension of sodium methylate the corresponding ester, according to reaction (D), is obtained. In a later paper<sup>5</sup> it will be shown that 3-bromo-3-methyl-4-heptanone behaves similarly. If alcoholic sodium methylate be allowed to react with 2-bromo-2-methyl-3-pentanone the hydroxy acetal is obtained in 65% yield, and no detectable amount of ester as would be expected.

The possibility that change of medium alone is the factor influencing the rearrangement to the ester is ruled out by the fact that if any alcohol is present a corresponding amount of hydroxy-acetal is obtained in the ether medium.

This consideration alone constitutes a compelling argument for an ethylene oxide intermediate for *both* rearrangements.

The fact that reaction (D) can compete with the last part of (C) when sodium ethylate

(4) Ward, *J. Chem. Soc.*, 1541 (1929).

(5) Greenburg, Burgess and Aston, to be published.

reacts in absolute ethanol perhaps may be associated with the larger size of the ethyl alcohol molecule, or at any rate with its lesser ability to cleave the ethylene oxide ring. Most certainly, given this fact, one would predict that with sodium isopropylate in isopropyl alcohol the ester would predominate. Such was actually observed.

The experiments of Ward<sup>4</sup> were the first to demonstrate the formation of a hydroxy-acetal instead of the alkoxy ketone, but as the compound he worked with had a phenyl group substituted on the  $\alpha$ -carbon of acetophenone the generality might be open to question. However, Bergmann and Mickely<sup>6</sup> obtained the methyl acetal of acetol by the action of sodium methylate in methanol on bromo-acetone, but it is important to note that they isolated no methoxy acetone. The only case we can find, where a normal product is obtained, is that reported by Henze and co-workers,<sup>7a,b</sup> in which chloracetone yields aryloxy derivatives with sodium phenolates in toluene. It must be for this reason that the alkoxy ketones reported have been prepared by other methods not involving direct metathesis, *e. g.*, the reaction of the alkoxy-nitrile with the appropriate Grignard reagent.

We tried unsuccessfully to methylate the hydroxy ketone. Methyl alcohol and hydrogen chloride, as well as dimethyl sulfate and aqueous alkali, gave no methylation product. In the latter case the ease of hydrolysis of the methoxy ketone may be the cause of its not being obtained. At any rate the dimethyl sulfate reacted rapidly but the hydroxy ketone was recovered unchanged. Moreover, when attempts were made to prepare the 2,4-dinitrophenylhydrazone of the hydroxy ketone in absolute alcohol, the derivative of the corresponding alkoxy ketone was obtained. Here hydrolysis is not possible, but the derivative is rapidly hydrolyzed by aqueous hydrochloric acid<sup>8</sup> to the 2,4-dinitrophenylhydrazone of the hydroxy ketone.

At the time our work was completed, a paper by Froning and Hennion<sup>9</sup> appeared with an independent synthesis of the hydroxy acetal II (R = Me) which is the hydroxy acetal we had obtained from 3-bromo-3-methyl-2-butanone by the action of sodium methylate in anhydrous methanol.

(6) Bergmann and Mickely, *Ber.*, **64**, 802 (1931).

(7) (a) Calaway and Henze, *This Journal*, **61**, 1355 (1939);  
(b) Whitney and Henze, *ibid.*, **60**, 1148 (1938).

(8) See also Schmidt and Austin, *Ber.*, **35**, 3721 (1902).

(9) Froning and Hennion, *This Journal*, **62**, 653 (1940).

The physical constants and derivatives they reported were the same as ours. This hydroxy acetal was treated with isopropylmagnesium bromide at room temperature. The only reaction was to replace the alcoholic hydrogen so that we recovered the acetal unchanged. However, using dibutyl ether solvent at 100° in the Grignard machine,<sup>10</sup> two molecules of methylmagnesium iodide reacted. Apparently the higher temperature caused one of the methoxy groups to be replaced.<sup>11</sup>

The results of the determination of the molecular weights of the hydroxy acetals by freezing point lowering in benzene deserve comment. The molecular weights are essentially normal, as was also observed by Froning and Hennion,<sup>9</sup> indicating absence of association. Fashion would dictate that this absence of association be attributed to internal hydrogen bonding of the alcoholic hydrogen with one of the ether oxygens. In this case we are inclined seriously to this point of view.

### Experimental

**3-Bromo-3-methyl-2-butanone** was prepared by the method of Favorskii.<sup>12</sup>

**3,3-Dimethoxy-2-methyl-2-butanol.**—A solution of sodium methylate was prepared by addition of 20.1 g. (0.875 mole) of sodium to 300 cc. of absolute methanol. The solution was cooled in ice and 145 g. (0.875 mole) of 3-bromo-3-methyl-2-butanone was added over a period of two hours. The solution was then allowed to come to room temperature with continued stirring and filtered. The precipitated sodium bromide was washed with methanol and the washings added to the filtrate. The methanol was taken off through a column to one-third volume, and the residue again filtered. Fractionation of the residual liquid gave 99.3 g. (76.5%) of colorless oil, b. p. 159–161° at 730 mm.;  $n_D^{20}$  1.4238;  $d_4^{20}$  0.968; *MR* (calcd.), 39.34; *MR* (obsd.) 39.10.

*Anal.* Calcd. for  $C_5H_{10}O(OCH_3)_2$ : C, 56.8; H, 10.8;  $OCH_3$ , 41.8. Found: C, 56.8, 56.8; H, 11.2, 11.3;  $OCH_3$ , 40.8.

**The 2,4-Dinitrophenylhydrazine Derivatives from the Hydroxy-acetal.**—Treatment with a solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid gave a derivative which when recrystallized from petroleum ether melted at 139–140° and did not depress the melting point of an authentic sample of the derivative of the hydroxy ketone prepared below.

*Anal.* Calcd. for  $C_{11}H_{14}N_4O_6$ : C, 46.8; H, 5.0. Found: C, 46.5; H, 5.3.

Treatment with 2,4-dinitrophenylhydrazine *in methanol* containing at the most only a trace of water and addition

(10) Kohler and Richtmyer, *ibid.*, **52**, 3738 (1930).

(11) Kranzfelder and Vogt, *ibid.*, **60**, 1714 (1938).

(12) Favorskii, *J. prakt. Chem.*, [2] **88**, 641 (1913).

of methanolic hydrochloric acid gave a derivative which when recrystallized from petroleum ether melted at 138–139° and did not depress the melting point of the derivative of 3-methoxy-3-methyl-2-butanone prepared below from the hydroxy ketone.

*Anal.* Calcd. for  $C_{11}H_{18}N_4O_4OCH_3$ :  $OCH_3$ , 10.5. Found:  $OCH_3$ , 10.0.

A mixed melting point of the two derivatives prepared above from the acetal was depressed to 112–114°.

**Hydrolysis of 3,3-Dimethoxy-2-methyl-2-butanol.**—Seventy-seven grams (0.52 mole) of the hydroxy acetal was placed with 50 cc. of 2% hydrochloric acid and refluxed for ninety minutes before fractionation through a twelve-plate column. Fractionation was continued up to a head temperature of 65°, giving 31.1 g. (0.97 mole) of methyl alcohol,  $n_D^{20}$  1.3282, or 94% of the theoretical amount. Saturation of the residue with potassium carbonate caused the separation of an oil layer, which was taken up in ether. The water was extracted with ether and the combined ether layers dried over anhydrous potassium carbonate and fractionated. This fractionation gave 48.6 g. (0.48 mole) of hydroxy ketone, b. p. 139–141°,  $n_D^{20}$  1.4155. This is 97% of the expected amount. The hydroxy ketone was identified as the semicarbazone, m. p. 164–165°.<sup>13</sup>

**3,3-Diethoxy-2-methyl-2-butanol.**—This compound was prepared by a reaction similar to that used for the methyl acetal, with the exception that after removal of the alcohol by distillation a small amount of water was added. The acetal layer was separated from the aqueous sodium bromide layer, dried and fractionated. A one mole run gave 54.4 g. (32.0%) of acetal, b. p. 110–112° at 98 mm.;  $n_D^{20}$  1.4189;  $d_4^{20}$  0.919; *MR* (calcd.) 48.57; *MR* (obsd.), 48.40.

*Anal.* Calcd. for  $C_9H_{20}O_3$ : C, 61.4; H, 11.4. Found: C, 61.5, H, 11.3.

From this reaction there was also isolated 17.6 g. (13.5%) of ethyl trimethylacetate, b. p. 59–62 at 100 mm. (see below).

#### 2,4-Dinitrophenylhydrazine Derivatives

This acetal gave derivatives in the same manner and with the same melting points as those prepared from the methyl acetal. From it a 2,4-dinitrophenylhydrazone was also prepared in absolute ethanol. It melted at 110.5–111°.

*Anal.* Calcd. for  $C_{11}H_{18}N_4O_6OEt$ : C, 50.3; H, 5.8;  $OEt$ , 14.5. Found: C, 50.3; H, 5.5;  $OEt$ , 14.3.

**Hydrolysis of 3,3-Diethoxy-2-methyl-2-butanol.**—A hydrolysis similar to that described above was carried out on 12.5 g. (0.071 mole) of the ethyl acetal. The recovery amounted to 86% of the theoretical ethanol, and 80% of the theoretical hydroxy ketone.

**3,3-Diisopropoxy-2-methyl-2-butanol.**—A preparation was carried out similar to those above using a solution of sodium isopropylate in isopropyl alcohol. The principal product of this reaction was isopropyl trimethylacetate, b. p. 49–51° at 46 mm. Since this product was unexpected, the distillation was not carried out under conditions which would give a satisfactory recovery of a low-boiling component. However, the isopropyl trimethylacetate isolated

amounted to 20%. The reaction also gave 8% of higher boiling material which was possibly the acetal, since it could be decomposed to give ketonic derivatives. The amount was too small to purify satisfactorily for analysis. It boiled from 67 to 95° at 46 mm. and had a refractive index of 1.4305–1.4382.

**Methyl Trimethylacetate from 3-Bromo-3-methyl-2-butanone.**—A suspension of sodium methylate in anhydrous ether was prepared by the addition of 11.5 g. of finely cut sodium (0.5 mole) to a solution of 30 cc. of methanol (0.75 mole) in 500 cc. of absolute ether. The solution was refluxed until solution of the sodium appeared to be complete, then addition of 82.5 g. (0.5 mole) of the bromo ketone was begun at such a rate as to cause continuous refluxing. After addition was complete the mixture was refluxed for one hour, then water was added in a quantity sufficient to dissolve all of the suspended solid. The ether layer was separated, dried over anhydrous sodium sulfate at 0° and fractionated to yield two fractions: Fraction A: 22 g., b. p. 31–45° at 100 mm.,  $n_D^{20}$  1.3870–1.3890; Fraction B: 12 g., b. p. 70–80° at 100 mm.,  $n_D^{20}$  1.4208–1.4248. Fraction A was identified as methyl trimethylacetate, yield 39%.

*Anal.* Calcd. for  $C_6H_{12}O_2$ : C, 62.0; H, 10.4; mol. wt., 114; neutr. equiv., 114. Found: C, 61.7; H, 10.3; mol. wt. (cryoscopic in benzene), 112, 113; neutr. equiv., 113.

Saponification gave methyl alcohol, identified as the 3,5-dinitrobenzoate, melting point and mixed melting point 105.5–107°, and trimethylacetic acid, melting point and mixed melting point 34–36°, amide, melting point and mixed melting point 153–154°.

Fraction B was evidently the hydroxy acetal, 3,3-dimethoxy-2-methyl-2-butanol, since upon treatment with acid it was decomposed to a compound which gave the 2,4-dinitrophenylhydrazone of 3-hydroxy-3-methyl-2-butanone, melting point and mixed melting point 138–139°. The formation of this product is probably due to the excess of alcohol used, since it does not appear in the preparation below where no excess of alcohol was used. The low yield of ester is no doubt due to the low temperature of fractionation, since vacuum was used to prevent decomposition of the product, whose nature was then unknown.

**Ethyl Trimethylacetate from 3-Bromo-3-methyl-2-butanone.**—A suspension of sodium ethylate in absolute ether was prepared by adding 11.5 g. (0.5 mole) of sodium and 29.2 cc. (0.5 mole) of absolute alcohol to 500 cc. of ether. The mixture was refluxed for forty-eight hours to ensure reaction and then cooled in ice and 82.5 g. (0.5 mole) of 3-bromo-3-methyl-2-butanone was added over a period of two hours. The solution was refluxed for three hours, then water was added to dissolve the precipitated sodium bromide. The layers were separated and the ether dried and fractionated. The yield was 39.8 g. (61.3%) of ester boiling at 116° at 725 mm.,  $n_D^{20}$  1.3912,  $d_4^{20}$  0.856, *MR* (calcd.) 36.18, *MR* (obsd.) 36.15.

*Anal.* Calcd. for  $C_7H_{14}O_2$ : C, 64.6; H, 10.8; mol. wt., 130; neutr. equiv., 130. Found: C, 64.4; H, 10.8; mol. wt. (cryoscopic in benzene), 129, 130; neutr. equiv. 138.

Saponification of a sample gave ethanol, identified as the 3,5-dinitrobenzoate, melting point and mixed melting point 91–92°, and trimethylacetic acid, m. p. 33–36°, amide, melting point and mixed melting point 153–154°.

(13) Freon, *Ann. chim.*, 11, 453 (1939).

**Isopropyl Trimethylacetate from 3-Bromo-3-methyl-2-butanone.**—This preparation was carried out exactly as that for ethyl trimethylacetate above, yielding 64% of ester in a one-half mole run. No acetal was found.

*Anal.* Calcd. for  $C_8H_{16}O_2$ : C, 66.6; H, 11.2; mol. wt., 144. Found: C, 66.4; H, 11.2; mol. wt. (cryoscopic in benzene), 141, 141.

Saponification of a sample gave trimethylacetic acid; amide, melting point and mixed melting point 152–154°.

**2-Bromo-2-methyl-3-pentanone** was prepared by bromination of ethyl isopropyl ketone, following the method given by Favorskii.<sup>12</sup>

**3,3-Dimethoxy-2-methyl-2-pentanol.**—This compound was prepared from 2-bromo-2-methyl-3-pentanone by the same procedure used above in the preparation of 3,3-dimethoxy-2-methyl-2-butanol. A one-half mole run gave 65.5% yield of an oil, b. p. 82.5° at 100 mm.,  $n_D^{20}$  1.4088,  $d_4^{20}$  0.8996, *MR* (calcd.) 43.96, *MR* (found) 44.54.

*Anal.* Calcd. for  $C_8H_{18}O_3$ : C, 59.3; H, 11.1. Found: C, 59.0, 59.1; H, 11.0, 11.1.

**2,4-Dinitrophenylhydrazine Derivatives from the Hydroxy-acetal.**—The 2,4-dinitrophenylhydrazone was prepared by the action of a saturated solution of the reagent in 2 *N* hydrochloric acid. Upon recrystallization from petroleum ether the derivative melted at 125–126°. This was the derivative of the hydroxy ketone as expected, and proved by a mixed melting point.

*Anal.* Calcd. for  $C_{12}H_{16}N_4O_8$ : C, 48.6; H, 5.4. Found: C, 48.2, 48.4; H, 5.7, 5.6.

A 2,4-dinitrophenylhydrazone was prepared in methanol containing at the most only a trace of water. Upon two recrystallizations from petroleum ether it melted at 139–139.5°. This was evidently the derivative of 2-methoxy-2-methyl-3-pentanone.

*Anal.* Calcd. for  $C_{13}H_{18}N_4O_8$ : C, 50.3; H, 5.8. Found: C, 50.1; H, 6.0.

A 2,4-dinitrophenylhydrazone was prepared in ethanol containing at the most only a trace of water. Upon recrystallization from petroleum ether it melted at 128–129°. This was evidently the derivative of 2-ethoxy-2-methyl-3-pentanone.

*Anal.* Calcd. for  $C_{14}H_{20}N_4O_8$ : C, 51.9; H, 6.2. Found: C, 51.6; H, 6.2.

A mixed melting point of the hydroxy and methoxy derivatives was depressed to 117–122°, a mixed melting point of the hydroxy and ethoxy derivatives was depressed to 108–114°.

In order to demonstrate that no rearrangement had occurred, the 2,4-dinitrophenylhydrazone of 3-methyl-3-hydroxy-2-pentanone was prepared. It melted at 86–87°, and a mixed melting point with a sample of the hydroxy derivative above (m. p. 125–126°) was depressed to below 70°. (For the preparation of 3-methyl-3-hydroxy-2-pentanone, see below.)

**Methyl Dimethylethylacetate from 2-Bromo-2-methyl-3-pentanone.** (By K. A. Burgess.)—This ester was obtained in 57% yield by a procedure similar to that given above for ethyl trimethylacetate, b. p. 125–126° at 730 mm.,  $n_D^{20}$  1.4021.

The acid was identified as the amide, m. p. 105–106°, mixed m. p. with an authentic sample, 102–103°.

**3-Hydroxy-3-methyl-2-butanone from Hydrolysis of 3-Bromo-3-methyl-2-butanone.**—Ninety-four grams (0.57 mole) of the bromo ketone was refluxed for one hour with a solution of 35.1 g. of potassium hydroxide (0.63 mole) in 250 cc. of water. Solution of the bromo ketone took place almost immediately, and at the end of the reaction only a very small amount of undissolved oil remained. The reaction mixture was saturated with sodium chloride and extracted with ether in a continuous extractor. The extraction was continued for one hundred hours, although less time probably would have been sufficient. The ether extract was dried with anhydrous magnesium sulfate, the ether stripped off and the residue fractionated to yield 46 g. (76%) of the hydroxy ketone, b. p. 140° at 727 mm.,  $n_D^{20}$  1.4155.

Acidification of a sample of the hydrolysis mixture gave no evidence of trimethylacetic acid, although this product might have been expected from the work of Favorskii and Bozhovskii.<sup>14</sup>

The semicarbazone was prepared in aqueous solution. After recrystallization from water it melted at 164–165° as reported by Freon.<sup>13</sup>

**The 2,4-Dinitrophenylhydrazine Derivatives from the Hydroxy Ketone.**—The 2,4-dinitrophenylhydrazone was prepared by the action of a saturated solution of the reagent in 2 *N* hydrochloric acid. After recrystallization from petroleum ether it melted at 138–139° and gave no depression when mixed with a sample of the 2,4-dinitrophenylhydrazone prepared above by the action of the aqueous reagent on 3,3-dimethoxy-2-methyl-2-butanol.

*Anal.* Calcd. for  $C_{11}H_{14}N_4O_8$ : C, 46.8; H, 5.0. Found: C, 46.6; H, 5.1.

A 2,4-dinitrophenylhydrazone was prepared in absolute methanol, using methanolic hydrochloric acid. The derivative was recrystallized from petroleum ether to a melting point of 138–139°. It did not depress the melting point of the 2,4-dinitrophenylhydrazone prepared above from 3,3-dimethoxy-2-methyl-2-butanol in a similar manner. It depressed the melting points of the derivatives of 3-hydroxy-3-methyl-2-butanone prepared from both the ketone and its acetal in aqueous media.

*Anal.* Calcd. for  $C_{11}H_{16}N_4O_8OCH_3$ :  $OCH_3$ , 10.5. Found:  $OCH_3$ , 10.0.

**2-Hydroxy-2-methyl-3-pentanone** was prepared in a manner similar to the above preparation of 3-hydroxy-3-methyl-2-butanone, in 70% yield. It boiled at 95–97° at 100 mm. as reported by Favorskii.<sup>12</sup>

**The 2,4-Dinitrophenylhydrazine Derivatives from the Hydroxy Ketone.**—The 2,4-dinitrophenylhydrazone was prepared by the action of a saturated solution of the reagent in 2 *N* hydrochloric acid. Upon recrystallization it melted at 125–126° and did not depress the melting point of the derivative prepared above from 3,3-dimethoxy-2-methyl-2-pentanol by the action of the same aqueous reagent.

A 2,4-dinitrophenylhydrazone was prepared in absolute methanol, with the addition of methanolic hydrochloric acid. It melted at 138–139° and did not depress the melting point of the derivative prepared from 3,3-dimethoxy-2-methyl-2-pentanol under similar conditions.

(14) Favorskii and Bozhovskii, *J. Russ. Phys.-Chem. Soc.*, **46**, 1097 (1914); *Chem. Abst.*, **9**, 1900 (1915).

**3-Bromo-3-methyl-2-pentanone** was prepared by bromination of methyl *s*-butyl ketone according to the method given by Favorskii<sup>12</sup> for 3-bromo-3-methyl-2-butanone. Fractionation of the product gave 40 g. of fore-run and 100 g. (56%) of product with b. p. 57° at 19 mm.,  $n^{20}_D$  1.4637,  $d^{20}_4$  1.3142,  $MR$  (calcd.) 37.56,  $MR$  (found) 37.68.

*Anal.* Calcd. for  $C_6H_{11}OBr$ : Br, 44.7. Found: Br, 44.4.

**3-Hydroxy-3-methyl-2-pentanone** was prepared by the hydrolysis of 19.8 g. (0.11 mole) of 3-bromo-3-methyl-2-pentanone with a solution of 8 g. (0.2 mole) of sodium hydroxide in 100 cc. of water. The reaction was refluxed for ten hours, then well extracted with ether. The ether layer was dried over anhydrous potassium carbonate and distilled to give 10.1 g. of product. The yield was 80%, b. p. 148–150° at 730 mm.,  $n^{20}_D$  1.4211,  $d^{20}_4$  0.9432,  $MR$  (calcd.) 31.19,  $MR$  (found) 31.44.

*Anal.* Calcd. for  $C_6H_{12}O_2$ : C, 62.4; H, 10.5. Found: C, 62.1; H, 10.4.

The 2,4-dinitrophenylhydrazone was prepared by the action of a solution of 2,4-dinitrophenylhydrazine in acidified 50% aqueous ethanol. After recrystallization from petroleum ether it melted at 86–87° and depressed the melting points of the derivatives of 2-hydroxy-2-methyl-3-pentanone prepared from the ketone and from the methyl acetal in aqueous media.

*Anal.* Calcd. for  $C_{12}H_{16}N_4O_5$ : C, 48.6; H, 5.4. Found: C, 48.3; H, 5.7.

**The Action of Isopropylmagnesium Bromide upon 3,3-Dimethoxy-2-methyl-2-butanol.**—A Grignard reagent was prepared in the usual manner from 49.2 g. (0.4 mole) of isopropyl bromide and 500 cc. of ether. To this solution was added 14.8 g. (0.1 mole) of the acetal. The addition took one hour, during which time gas was evolved continuously. After completion of the addition the solution was refluxed and stirred for one hour. It was then decomposed by cautious addition of water and the ether layer decanted. The residue was steam distilled, the distillate extracted with ether and the ether layers combined. The ether was dried over anhydrous potassium carbonate and distilled. Eleven and one-half grams of oil was obtained boiling at 37–39° at 1 mm. This oil was analyzed for methoxyl.

*Anal.* Calcd. for 3,3-dimethoxy-2-methyl-2-butanol: OMe, 41.8. Found: OMe, 40.0. Apparently the acetal came through the reaction unchanged, as the analysis shows.

A 2,4-dinitrophenylhydrazone of this product was prepared by the action of a saturated solution of the reagent in 2 *N* hydrochloric acid. Melting point and mixed melting point with an authentic sample of the derivative from 3-hydroxy-3-methyl-2-butanone was 138–139°.

**The Action of Methanolic Hydrochloric Acid on 3-Hydroxy-3-methyl-2-butanone.**—Ten grams (0.1 mole) of 3-hydroxy-3-methyl-2-butanone was placed in a 50-cc. flask with 10 cc. (0.25 mole) of absolute methanol. To this mixture was added 5 drops of a saturated solution of hydrochloric acid in methanol and the mixture refluxed for one hour with protection from external moisture. Neutralization and distillation gave 9.2 g. of methanol boiling between 63.5 and 75° and two arbitrary higher boiling fractions, (2.0 g., b. p. 135–138°,  $n^{20}_D$  1.4070; and 7.0 g., b. p. 138–139°,  $n^{20}_D$  1.4155). Semicarbazones were prepared from both fractions, using a solution of semicarbazide

hydrochloride buffered with sodium acetate. Both derivatives melted at 164–165°, the same as that of the starting material. A mixed melting point was not depressed.

**The Action of Dimethyl Sulfate upon 3-Hydroxy-3-methyl-2-butanone.**—A solution of 37.1 g. (0.36 mole) of the hydroxy ketone in 150 cc. of water was prepared. To this was added 16.0 g. (0.4 mole) of sodium hydroxide and the resulting solution cooled in an ice-bath. The solution was stirred mechanically and 22.9 g. (0.2 mole) of dimethyl sulfate added dropwise over a period of one hour. The mixture was stirred for three additional hours and then steam distilled. Seventy-five cc. of distillate was collected, including 5 cc. of an oil layer, lighter than water. The distillate was saturated with potassium carbonate and well extracted with ether. The ether layer was dried over anhydrous potassium carbonate and fractionated to give 27 g. of a product boiling at 138° and having a refractive index of 1.4152–1.4155. These constants are those of the starting material. A semicarbazone was prepared in the same manner as in the experiment immediately above. The melting point, and mixed melting point with a sample prepared from the starting material, was 164–165°.

### Summary

1. The action of sodium methylate on 3-bromo-3-methyl-2-butanone in absolute methanol gives the methyl acetal of 3-hydroxy-3-methyl-2-butanone as expected.
2. Sodium ethylate and sodium isopropylate behave similarly but also give some of the corresponding ester of trimethylacetic acid.
3. Suspensions of the sodium alcoholates from methyl, ethyl and isopropyl alcohols in ether solution of this bromo ketone act to yield the ester of trimethylacetic acid corresponding to the alcohol used.
4. When there was excess methyl alcohol in the suspending ether both the methyl acetal of the hydroxy ketone and methyl trimethylacetate were obtained by the action of sodium methylate.
5. Definitive evidence has been obtained that an ethylene oxide structure is an intermediate common to both types of rearrangement.
6. 2-Bromo-2-methyl-3-pentanone gives the methyl acetal of the hydroxy ketone with sodium methylate in absolute methanol. When a suspension of sodium methylate in anhydrous ether is used methyl dimethylethylacetate is the sole product, thus indicating the generality of a reaction which may prove useful as a method of synthesis of trialkylacetic acids.
7. The hydroxy acetals are readily converted into alkoxy-ketone 2,4-dinitrophenylhydrazones when the derivative is prepared in a practically anhydrous alcohol.