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

Anomalous Oxidation of Some Secondary Alcohols Containing an α-Neo Carbon[1]

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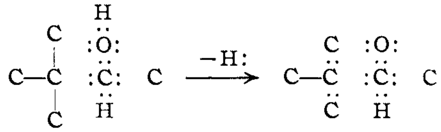
The oxidation of secondary alcohols with such reagents as chromic anhydride in acetic acid solution generally gives good yields of the corresponding ketones. In connection with the preparation of methyl *t*-amyl ketone for use in the synthesis of 2,3,4-trimethylhexane[2] an unexpected product was isolated. The oxidation of methyl-*t*-amylcarbinol with chromic anhydride in acetic acid, containing about 20% water, gave 7% *t*-amyl alcohol in addition to the desired ketone. The same reaction with methyl-*t*-butylcarbinol gave 6% *t*-butyl alcohol, and isopropyl-*t*-amylcarbinol gave 7% *t*-amyl alcohol.

Although this preliminary work is not sufficiently comprehensive to permit any generalization as to this type of reaction, the indications are that complete substitution on the carbon *alpha* to the hydroxyl-bearing carbon leads to unusual behavior on oxidation with chromic anhydride. Probably other alcohols with a lower degree of substitution behave in a similar manner, but greater susceptibility of the alcohols which might be formed to oxidative attack prevents their isolation. It is believed that the complete elucidation of the formation of the tertiary alcohols in this unexpected oxidation may well be the key to all oxidative carbon-to-carbon single bond ruptures in oxygenated organic compounds in polar solvents. Related studies are now under way.

From the standpoint of mechanism, the first question is whether the tertiary alcohols are formed from the carbinol or from the ketone formed in the oxidation. The oxidation of pinacolone with dichromate and acid has been studied by Friedel and Silva[3] and by Butlerow[4] who found that trimethylacetic acid was formed. We have repeated this oxidation using chromic anhydride as employed in the above alcohol oxidations. While the oxidation of the alcohols is rapid at 30° no oxidation of the pinacolone is apparent until temperatures close to 100° are reached. Only trimethylacetic acid could be isolated although any *t*-butyl alcohol which might have been formed would probably have been further oxidized. The great difference in ease of oxidation of ketones and carbinols, which is well known, points to a different mechanism and favors the belief that the fission to the tertiary alcohols occurs in the carbinol rather than in the ketone.

The following tentative mechanism for the cleavage exemplified with pinacolone, is suggested. The oxidizing agent abstracts a hydrogen with an electron pair (a hydride ion) from the hydroxyl group. Certainly the hydrogen of the hydroxyl is the most polar hydrogen in the molecule so that the energetics would favor approach of the oxidizing agent. The great difficulty with which ethers are oxidized by reagents, other than oxygen, is also in harmony.



I II

The intermediate ion II, which would be expected to show many carbonium ion type reactions, can be stabilized intramolecularly in two ways. First, a proton may be expelled followed by rearrangement of an electron pair to create a carbonyl group. This process is apparently the chief one because of the high yields of ketones obtained. The second possibility depends on the fact that the electronically deficient oxygen atom exerts a powerful attraction for the electron pair joining the *t*-butyl group to the oxygenated carbon atom, while the *t*-butyl has a low attraction for these same electrons.[5] The configuration here, R_3C-C-O^+, is analogous to that found by Whitmore and Stahly to be critical for the acid catalyzed depolymerization of branched olefins,[6] R_3C-C-C^+. If this electron pair is appropriated by the oxygen, rupture of the molecule occurs to form a tertiary carbonium ion and a molecule of aldehyde. Both stabilization processes are summarized in Fig. 1. We have made the assumption that the normal product of the reaction, the ketone, and the abnormal product, the tertiary alcohol, have come from a common intermediate. There is no direct evidence for this, and later work may possibly show that two independent mechanisms are involved.

The carbonium ion formed in the cleavage may react with water: $(CH_3)_3C^+ + HOH \rightleftarrows (CH_3)_3COH + H^+$. Reaction with acetic acid to give *t*-butyl acetate might also take place, but such esters are hydrolyzed very readily in acidic solutions.[7] At higher temperatures olefin would be expected through the expulsion of a proton from the tertiary carbonium ion and this has been found to be the case.[8] The experimental conditions used in

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[1] Presented in part before the Organic Division, American Chemical Society, New York, N. Y., September, 1944.

[2] Whitmore, Organic Division, American Chemical Society, Cleveland, April, 1944.

[3] Friedel and Silva, *Compt. rend.*, **76**, 230 (1873); *Ber.*, **6**, 146, 826 (1873); *Bull. Soc. Chim.*, [2] **19**, 193 (1873).

[4] Butlerow, *Ann.*, **170**, 168 (1873).

[5] Whitmore and Bernstein, THIS JOURNAL, **60**, 2626 (1938).

[6] Whitmore and Stahly, *ibid.*, **55**, 4153 (1933); **68**, 281 (1946).

[7] Cohen and Schneider, *ibid.*, **63**, 3382 (1941).

[8] N. C. Cook, The Pennsylvania State College, private communication.

this work would oxidize any aldehyde which might be formed. Aldehydes have been isolated under modified conditions, however, and the description of that work will be published later.

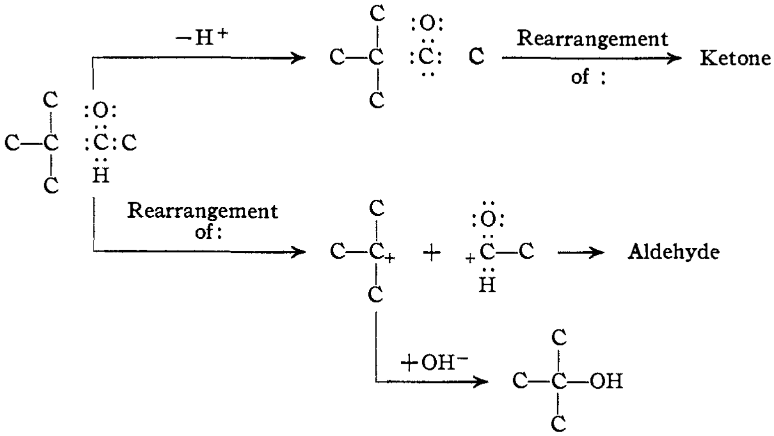

Fig. 1.

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Experimental

Materials.—Methyl-*t*-amylcarbinol was prepared from *t*-amylmagnesium chloride and acetaldehyde, methyl-*t*-butylcarbinol from *t*-butylmagnesium chloride and acetaldehyde and isopropyl-*t*-amylcarbinol from isopropylmagnesium bromide and dimethylethylacetyl chloride, employing the usual procedures. All products were fractionated through columns of 12–15 theoretical plates. One sample of methyl-*t*-butylcarbinol was prepared by the catalytic reduction of pinacolone prepared from acetone. Further details will be published with the original investigation.[2]

Oxidation of Alcohols.—All oxidations were carried out in the following manner, exemplified with methyl-*t*-amylcarbinol. In a 3-necked 3-liter flask 336 g. of methyl-*t*-amylcarbinol (2.9 moles, n^{20}_D 1.4300) was dissolved in 150 ml. of glacial acetic acid. The flask was equipped with a stirrer, dropping funnel, and thermometer. Two moles (200 g.) of chromic anhydride was dissolved in 100 ml. of water and 250 ml. of glacial acetic added when solution in the water was complete. The chromic anhydride solution was added dropwise to the carbinol over a period of eight hours with the temperature below 30° at all times. The product was diluted with 2 liters of water and the ketone layer separated and washed with bicarbonate solution and then water. The water layer from the reaction was steam-distilled after the addition of 20 ml. of ethyl alcohol to react with any unused oxidant. The oil layer from the steam distillate was combined with the main portion after washing as before. The crude ketone was dried over potassium carbonate which also served to remove any acids present. The dry product was fractionated through a column equivalent to 15 theoretical plates.

Identification of Products.—From each oxidation early distillation cuts were obtained with physical properties corresponding to *t*-amyl or *t*-butyl alcohol. It was the characteristic odor of these cuts which prompted further study. These suspected cuts were treated with concentrated hydrochloric acid and the chlorides obtained, after checking density and index of refraction, were converted to the Grignard reagents, and these reacted with phenyl isocyanate to give, respectively, *t*-amylacetanilide, m. p. and mixed m. p. 105–106°, and *t*-butylacetanilide, m. p. and mixed m. p. 132°. The tertiary alcohol cuts from methyl-*t*-butyl-, methyl-*t*-amyl-, and isopropyl-*t*-amylcarbinols were, respectively, 6, 7 and 7%. The yields of ketone obtained were 70–75%. Three separate oxidations were made with methyl-*t*-amylcarbinol and two with methyl-*t*-butylcarbinol; the results were identical. The yield of *t*-butyl alcohol from methyl-*t*-butylcarbinol prepared from pinacolone was the same as the yield from the product made through the Grignard reaction.

Oxidation of Pinacolone.—Pinacolone was prepared according to "Organic Syntheses."[9] Oxidation was carried out as in the case of methyl-*t*-amylcarbinol above. Oxidation did not take place at 50 or 80°, but did proceed at 100°. After five hours the reaction mixture was diluted and steam distilled. Basic reagents were avoided. Fractionation gave 75% trimethylacetic acid (b. p. 164° (760 mm.), anilide m. p. and mixed m. p. 129°) and 18% unreacted ketone. No tertiary butyl alcohol was detected.

Summary

1. Oxidation of methyl-*t*-amylcarbinol and isopropyl-*t*-amylcarbinol with chromic anhydride in acetic acid gives in both cases 7% *t*-amyl alcohol. Similarly methyl-*t*-butylcarbinol gives 6% *t*-butyl alcohol.

2. These tertiary alcohols are formed from the carbinols as the oxidation of pinacolone does not take place under similar conditions and under more drastic conditions yields trimethylacetic acid.

3. A mechanism involving the removal of a hydride ion from the hydroxyl group to give an intermediate ion with an electronically deficient oxygen is proposed. The tertiary alcohols are obtained by rearrangement of an electron pair without the attached group, while ketones, the principal products, are obtained by expulsion of proton from the intermediate.

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[9] "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., pp. 459, 462.