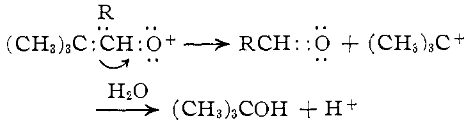
Further oxidation of the keto alcohol results in the final product, $C_6H_5CO(CH_2)_4COOH$.[21]

In the oxidation of alcohols, the reaction appears always to go through the intermediate stage of ester formation. For example, when CrO_3, HNO_3, $S_2O_8^{=}$, HOCl or HIO_4 is the oxidizing agent, the esters formed are, respectively, $ROCrO_3H$, $RONO_2$, $ROOSO_3H$, ROCl and $ROIO_3$. These intermediate esters are relatively stable only when R is a tertiary alkyl group; the primary and secondary esters decompose in the cold and are violently explosive on heating.[22] The reason for this is that the subsequent oxidative steps can proceed rapidly when a proton can be expelled from the incipiently forming ions $RCH_2{:}\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}}{}^+$ or $R_2CH{:}\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}}{}^+$, whereas a tertiary ester can expel only a carbonium ion (R^+) from $R_3C{:}\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}}{}^+$, which is, energetically, more difficult to do. Thus, *t*-butyl hypochlorite,[23] and chromate[24] are surprisingly stable.

The formation of carbonium ions in the oxidative cleavage of tertiary alcohols, ketones and acids[25] is implicit in the generalized approach to organic oxidation presented here. Even primary and secondary alcohols might be expected to expel carbonium ions in competition with proton ejection when the carbonium ion (such as $(CH_3)_3C^+$ or $C_6H_5CH_2^+$) is one that can be formed readily because of its relative stability. Such cleavage actually has been observed in the case of chromic acid oxidation of methyl-*t*-butylcarbinol to *t*-butyl alcohol and acetaldehyde[26] and of phenyl-*t*-butylcarbinol to *t*-butyl alcohol and benzaldehyde.[27] The mechanism of the cleavage is easily explained on the basis of the present view, and may be simply represented as



$$(CH_3)_3C{:}\overset{R}{\ddot{C}H}{:}\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}}{}^+ \longrightarrow RCH{::}\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}} + (CH_3)_3C^+ \xrightarrow{H_2O} (CH_3)_3COH + H^+$$

If carbonium ions of sufficiently long half-life are actually ejected from molecules undergoing oxidative fission of C–C bonds, one might expect that rearrangements involving certain of them would have been noted. Such molecular rearrangements have in fact been observed, for example in the chromic acid oxidation of cycloöctatetraene[28] to *p*-phthalic acid, and in the permanganate oxidation of camphene[29] to camphenic acid.[30] Both of these reactions may be explained[31] readily on the basis outlined here.

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[21] L. F. Fieser and M. Fieser, "Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1950, p. 709.

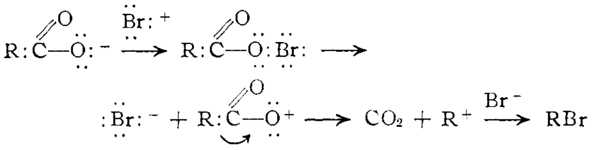
[22] F. C. Whitmore, "Organic Chemistry," D. Van Nostrand, New York, N. Y., 1951, p. 156–158.

[23] D. Ginsberg, *Experientia*, **7**, 95 (1951); L. F. Audrieth, E. Colton and M. M. Jones, THIS JOURNAL, **76**, 1428 (1954).

[24] R. V. Oppenauer and H. Oberrauch, *Anales Asoc. quim. argentina*, **37**, 246 (1949).

[25] Oxidative decarboxylation of acids may well proceed through the formation of an acyl ester, RCOOX, as the intermediate. The acyl nitrates and bisulfates have been isolated, though they are very unstable (ref. 22, p. 293). A typical example of such an oxidative fission is the decarboxylation of silver salts, $RCOO^-Ag^+$, by reaction with bromine (E. Maekawa, *C. A.*, **48**, 1245f (1954)). The mechanism appears to be

$$Ag^+ + Br_2 \longrightarrow \overset{+\ -}{AgBr} + Br^+$$



[26] W. A. Mosher and F. C. Whitmore, THIS JOURNAL, **70**, 2544 (1948).

[27] A. Leo and F. H. Westheimer, *ibid.*, **74**, 4383 (1952).

[28] E. E. Royals, "Advanced Organic Chemistry," Prentice–Hall, Inc., New York, N. Y., 1954, p. 547.

[29] Ref. 22, p. 581.

[30] A striking confirmation of the carbonium ion nature of the cleaved group has been established recently in the chromic acid oxidation of *l*-3-methyl-3-phenyl-2-pentanol, in which the expelled carbonium ion was completely racemized to give *d,l*-2-phenyl-2-butanol (W. A. Mosher and S. Duckworth, Abstracts of Papers, Cincinnati Meeting of A.C.S., April 2, 1955, p. 46N).

[31] L. S. Levitt, *J. Org. Chem.*, in press.

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NOTES

The Oxidation of Tungsten Carbide

By ARTHUR E. NEWKIRK

RECEIVED APRIL 14, 1955

Tungsten carbide powder is known to burn in air, but information about the ignition temperature and rate of combustion seems lacking. For analytical combustion it is common to use high temperatures, oxygen and a flux, although rapid direct combustion can be achieved at approximately 1400° in oxygen.[1] The present thermobalance studies show that fine tungsten carbide powder begins to oxidize rapidly in air at 500 to 520°, and can be burned completely at 529°.

The materials used were: (1) a tungsten carbide powder supplied by the Carboloy Department of the General Electric Company. This material contained 6.24 ± 0.04% C, or 0.11% more than theoretical.[1] (2) A macrocrystalline tungsten carbide obtained from the Wah Chang Corporation. Samples of these materials were weighed into porcelain crucibles and heated at a rate of 300°/hr. (unless otherwise noted) in a pen-recording Chevenard thermobalance. This instrument, manufactured by Société Adamel, is similar in principle and operation to that described by Duval.[2]

The curves from four experiments are shown in

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[1] E. L. Simons, J. E. Fagel, Jr., and E. W. Balis, *Anal. Chem.*, in press.

[2] C. Duval, "Inorganic Thermogravimetric Analysis," Elsevier Publishing Co., New York, N. Y., 1953, Part 1, Chapter 2.

the figure. On close examination, the curves for sample 1 reveal a 1-to-2 mg. uniform weight increase up to approximately 450°. Sample 2 shows a loss of the same magnitude. Above 450° the samples gain weight at a lowly increasing rate, and at about 515° a rapid weight gain begins. The onset of rapid oxidation occurs at a higher temperature for the coarser sample.

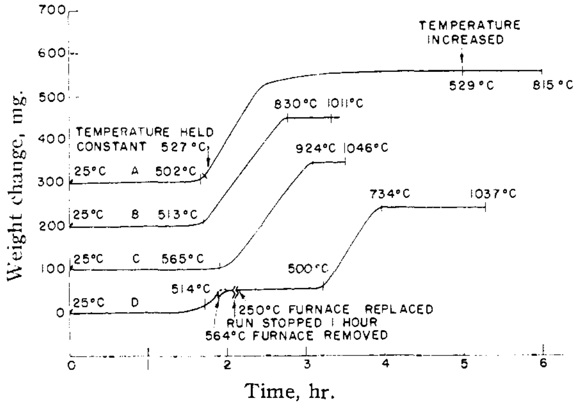

Fig. 1.—A, B and D, sample 1, carbon = 6.15, 6.26, 6.24%; C, sample 2, carbon = 6.20%.

In run A, the weight gain during uniform rapid burning at constant temperature was 4.8 mg. per minute. In run D the weight change after partial combustion indicated that 22% of the sample had burned. The per cent. carbon for each run was computed from the final weight change assuming the residue to be WO_3.

I wish to acknowledge helpful discussions with Dr. E. I. Simons, and assistance from Miss I. Aliferis in measuring some of the curves.

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The Ionization Constants of the Heme-Linked Groups of Hemoglobin[1]

BY ROBERT A. ALBERTY

RECEIVED MARCH 17, 1955

Wyman[2] has shown how the equilibria of hemoglobin involving protons and molecular oxygen may be treated from a unified point of view by means of the theory for linked functions. It was shown that the differential titration data of Wyman and co-workers[3,4] and the *p*H variation of the oxygen tension as measured by Ferry and Green[5] could be interpreted quantitatively in terms of the ionization constants of two heme-linked groups. Upon oxygenation one of these groups is rendered stronger and the other weaker. It is the purpose of this note to show that one of the assumptions made by Wyman—namely, that the ionizations of these two groups are independent of each other—is unnecessary for a quantitative treatment.

Theory.—The part of hemoglobin (P) which affects the oxygen binding may be represented as a dibasic acid HPH, where one proton has been written to the left, and the other to the right, to distinguish between the two acidic groups. Since the first proton may dissociate from either position the resulting equilibria[6] may be represented by

$$\begin{tikzcd}
\mathrm{HPO_2} \arrow[rrr, shift left, "k_3''"] \arrow[ddd, shift left] \arrow[dr, shift left] & & & \mathrm{PO_2} \arrow[lll, shift left] \arrow[ddd, shift left, "k_4''"] \arrow[dl, shift left] \\
& \mathrm{HP} \arrow[r, shift left, "k'_3"] \arrow[d, shift left] \arrow[ul, shift left] & \mathrm{P} \arrow[l, shift left] \arrow[d, shift left, "k_4'"] \arrow[ur, shift left] & \\
& \mathrm{HPH} \arrow[r, shift left] \arrow[u, shift left, "k_1'"] \arrow[dl, shift left] & \mathrm{PH} \arrow[l, shift left, "k'_2"] \arrow[u, shift left] \arrow[dr, shift left] & \\
\mathrm{HPHO_2} \arrow[uuu, shift left, "k_1''"] \arrow[rrr, shift left] \arrow[ur, shift left] & & & \mathrm{PHO_2} \arrow[lll, shift left, "k_2''"] \arrow[uuu, shift left] \arrow[ul, shift left]
\end{tikzcd} \qquad (1)$$

where the *k*'s are the microscopic acid dissociation constants which are not subject to direct measurement in the absence of means for distinguishing between isomers such as HP and PH. For example, $k_1' = (H^+)(HP)/(HPH)$, $k_3' = (H^+)(P)/(HP)$. These microscopic constants are not all independent since $k_1'k_3' = k_2'k_4'$ and $k_1''k_3'' = k_2''k_4''$.

In interpreting the experimental data for hemoglobin Wyman assumed that the two ionizable groups are independent. This amounts to setting $k_3' = k_2'$, $k_4' = k_1'$, $k_3'' = k_2''$ and $k_4'' = k_1''$. On the basis of this assumption the number, $\Delta\bar{X}$, of equivalents of acid produced per heme upon complete oxygenation is

$$\Delta\bar{X} = \frac{k_1''}{(H^+) + k_1''} + \frac{k_2''}{(H^+) + k_2''} - \frac{k_1'}{(H^+) + k_1'} - \frac{k_2'}{(H^+) + k_2'} \qquad (2)$$

On the basis of the same assumption the oxygen pressure, $p_{1/2}$, required for half saturation is given by

$$p_{1/2} = (\text{const.}) \frac{[(H^+) + k_1'][(H^+) + k_2']}{[(H^+) + k_1''][(H^+) + k_2'']} \qquad (3)$$

The values of k_1', k_2', k_1'' and k_2'' obtained by Wyman from these two types of experimental data are listed in Table I under assumption (a).

The assumption of the independence of the ionizable groups upon which equations 2 and 3 are based is not required for a mathematical treatment and imposes a limitation which is undesirable since the two ionizable groups are presumably close to the heme and might be expected to have an effect on each other.

For a more general treatment the equilibria may be written as

$$\begin{tikzcd}
\mathrm{P} \arrow[d, shift left] & & \mathrm{PO_2} \arrow[d, shift left, "K_2''"] \\
\mathrm{PH} + \mathrm{O_2} \arrow[u, shift left, "K_2'"] \arrow[d, shift left] \arrow[rr, shift left, "K_{O_2}"] & & \mathrm{PHO_2} \arrow[ll, shift left] \arrow[u, shift left] \arrow[d, shift left, "K_1''"] \\
\mathrm{PH_2} \arrow[u, shift left, "K_1'"] & & \mathrm{PH_2O_2} \arrow[u, shift left]
\end{tikzcd} \qquad (4)$$

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[1] This research was supported by a grant from the National Science Foundation and a research grant-in-aid from the du Pont Company.

[2] J. Wyman, in M. L. Anson and J. T. Edsall, "Advances in Protein Chemistry," Vol. IV, Academic Press, Inc., New York, N. Y., 1948, p. 407.

[3] B. German and J. Wyman, *J. Biol. Chem.*, **117**, 533 (1937).

[4] J. Wyman and E. N. Ingalls, *ibid.*, **139**, 877 (1941).

[5] R. M. Ferry and A. A. Green, *ibid.*, **81**, 175 (1929).

[6] E. Q. Adams, THIS JOURNAL, **38**, 1503 (1916).