CHAPTER 3

THE BAEYER-VILLIGER OXIDATION OF ALDEHYDES AND KETONES

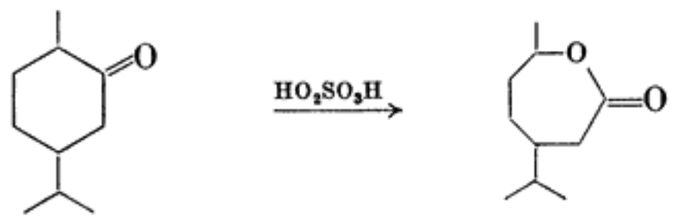
C. H. HASSALL

University College of the West Indies, Jamaica

CONTENTS

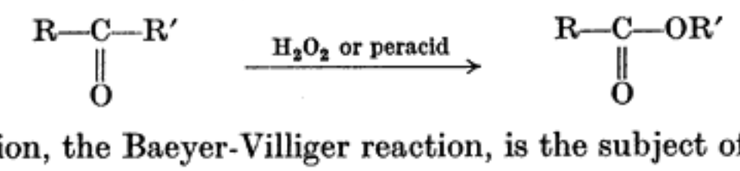
INTRODUCTION

In 1899, Baeyer and Villiger[1] showed that the oxidation of the alicyclic ketones menthone, tetrahydrocarvone (I), and camphor with permonosulfuric acid led to the formation of lactones.



I

Further studies, using a variety of ketones or aldehydes and hydrogen peroxide or peracids in various media, have established that the oxidation represented by the following equation is of wide applicability.



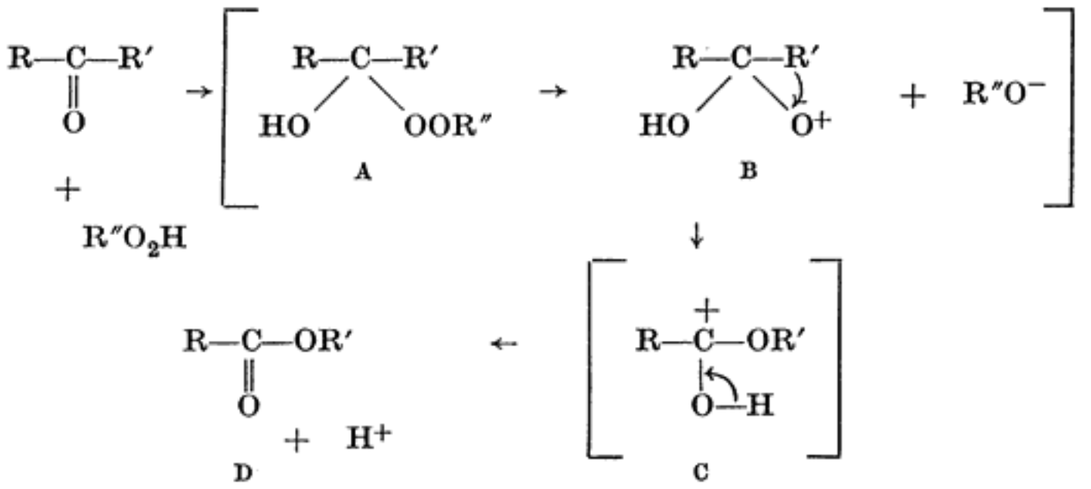
This oxidation, the Baeyer-Villiger reaction, is the subject of this review. As the oxidation normally employs mild conditions, gives reasonable yields, and shows a high degree of selectivity, it has proved useful in a variety of both synthetic and degradative studies. Recent investigations have led to a better definition of favorable experimental conditions and have extended appreciably the scope of the reaction.

MECHANISM OF THE REACTION

It is now generally agreed that the Baeyer-Villiger reaction is ionic in character. The favored reaction pattern was first outlined by Criegee in 1948.[2] It assumes that in the first instance addition of the peroxide to the carbonyl group yields a hydroxyperoxide (A). This dissociates to give an electron-deficient ion (B), which rearranges to C with cleavage of a carbon-carbon bond. The postulated carbonium ion C decomposes to the ester D in a normal way.

This mechanism has recently been the subject of detailed discussion by a number of authors.[3–9] The scheme accounts for the observation that in the oxidation of substituted acetophenones with perbenzoic acid the

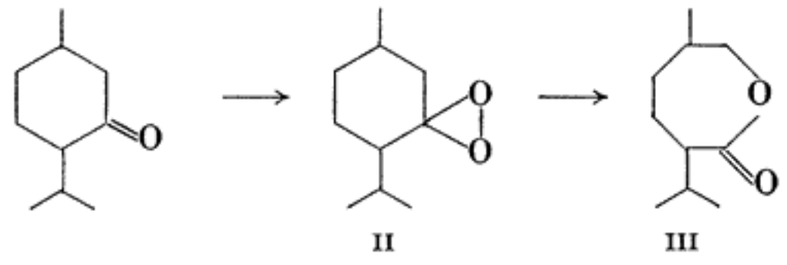
[1] Baeyer and Villiger, *Ber.*, **32**, 3625 (1899).
[2] Criegee, *Ann.*, **560**, 127 (1948).



rate-determining step is the acid-catalyzed addition of perbenzoic acid to the carbonyl group.[10] It recognizes that in certain cases hydroxyhydroperoxides have been isolated and converted to rearrangement products by heating alone.[11] It explains the fact that the migratory aptitude of aryl groups R, R′ is normally proportional to their capacity for electron release.[4] There is a general similarity of the mechanism to those postulated, inter alia, for the Beckmann, pinacol-pinacolone, Hofmann,[12] Curtius,[12] Wagner-Meerwein, and acid-catalyzed hydroperoxide rearrangements.[13]

There is, however, no explicit evidence for an intermediate ion having six electrons and a positive charge on oxygen. The reaction sequence illustrated could take place without the occurrence of B as an intermediate if the steps from A to B and B to C were concerted.

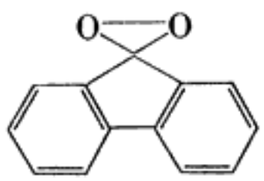
In their discussion of the reaction Baeyer and Villiger[1] suggested that the simple "oxoxide" II participated as an intermediate in the oxidation of menthone to the lactone III. Until recently it appeared that this was



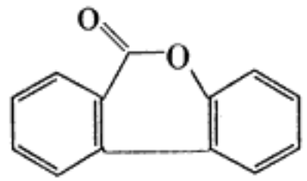
II III

[3] Doering and Dorfman, *J. Am. Chem. Soc.*, **75**, 5595 (1953).
[4] Doering and Speers, *J. Am. Chem. Soc.*, **72**, 5515 (1950).
[5] Friess, *J. Am. Chem. Soc.*, **71**, 2571 (1949).
[6] Leffler, *J. Org. Chem.*, **16**, 1785 (1951).
[7] Turner, *J. Am. Chem. Soc.*, **72**, 879 (1950).
[8] Karrer and Haab, *Helv. Chim. Acta*, **32**, 950 (1949).
[9] Robertson and Waters, *J. Chem. Soc.*, **1948**, 1574.
[10] Friess and Soloway, *J. Am. Chem. Soc.*, **73**, 3968 (1951).
[11] Späth, Pailer, and Schmid, *Ber.*, **74**, 1552 (1941).
[12] Wallis and Lane, *Org. Reactions*, **3**, 267–306 (1946).
[13] Bartlett and Cotman, *J. Am. Chem. Soc.*, **72**, 3095 (1950).

supported by the observation that fluorenone peroxide, formulated as IV, rearranged to the lactone V on heating.[14] There is now evidence that fluorenone peroxide is a molecular complex of fluorenone and fluorenone hydroperoxide.[15] There is no evidence for the existence of stable "oxoxides."



IV



V

It has been postulated that hydroxyl radicals may participate in the oxidation by interacting with the enolic form of the ketone.[16] It is unlikely that such a step is involved in the Baeyer-Villiger reaction, as many ketones that are not capable of enolization undergo the reaction. Also, in cases where it is established that attack on enols takes place, hydroxylation and not Baeyer-Villiger oxidation occurs.[17] It has been shown that unsaturated ketones may undergo Baeyer-Villiger oxidation without the olefinic bonds being attacked.[18] This would not be expected if free hydroxyl radicals were involved.[19]

SCOPE OF THE REACTION

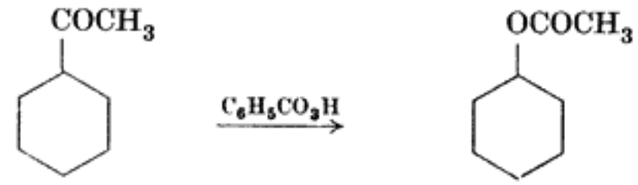
Saturated Aliphatic Ketones. There is only one example of the Baeyer-Villiger oxidation of a simple ketone of the type RCH_2COCH_2R' to an ester. Methyl *n*-hexyl ketone gives *n*-hexyl acetate (VI) and its hydrolysis products on treatment with hydrogen peroxide in hydrofluoric acid.[20]

$$CH_3(CH_2)_5COCH_3 \xrightarrow[HF]{H_2O_2} \underset{VI}{CH_3(CH_2)_5OCOCH_3} + CH_3CO_2H + CH_3(CH_2)_5OH$$

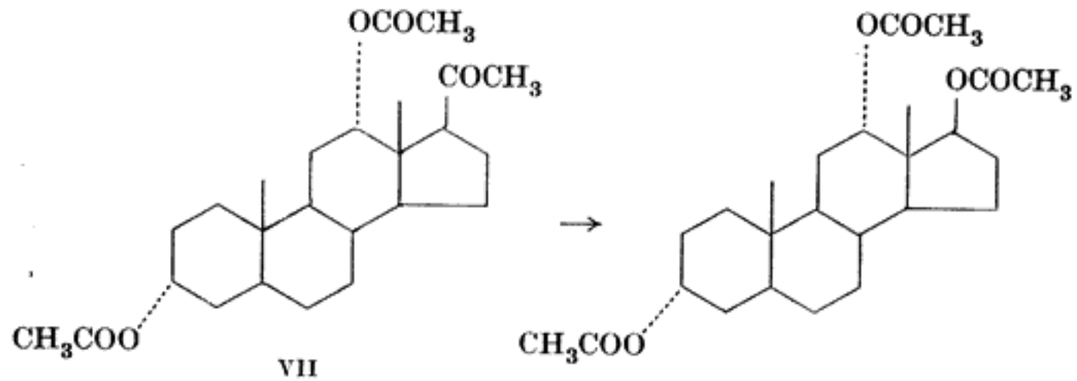
It has been shown that hydrogen peroxide in the presence of sulfuric acid may oxidize such ketones to ketone peroxides and α-ketols.[21] Perbenzoic acid is said to have no significant action.[22] However, as peracids have not yet been used under the most favorable conditions there is no decisive evidence that they will not react with these simple ketones.

[14] Wittig and Pieper, *Ber.*, **73**, 295 (1940).
[15] Criegee, Schnorrenberg, and Becke, *Ann.*, **565**, 7 (1949).
[16] Böeseken, *Proc. Acad. Sci. Amsterdam*, **33**, 134 (1930) [*C. A.*, **24**, 3806 (1930)].
[17] Kritchevsky and Gallagher, *J. Biol. Chem.*, **179**, 507 (1949).
[18] Karrer and Schneider, *Helv. Chim. Acta*, **30**, 859 (1947).
[19] Baxendale, Evans, and Park, *Trans. Faraday Soc.*, **42**, 155 (1946).
[20] Hudlecky, *Chem. Listy*, **45**, 380 (1952) [*C. A.*, **47**, 8012 (1953)].
[21] Pastureau, *Compt. rend.*, **140**, 1592 (1905); *Bull. soc. chim. France*, [4] **5**, 227 (1909).
[22] Baeyer and Villiger, *Ber.*, **33**, 1569 (1900).

When ketones with the carbonyl group attached to at least one secondary carbon atom are treated with peracids, esters are formed. The secondary grouping rearranges in preference to a primary one. In the series of alicyclic methyl ketones from methyl cyclobutyl ketone to methyl cycloheptyl ketone, oxidation with perbenzoic acid gives yields of acetates ranging from 58 to 78%.[23]



Steroid alcohols with the hydroxyl group attached to C–17 may be prepared conveniently by the Baeyer-Villiger oxidation of 20-keto steroids, such as pregnan-3α,12α-diol-20-one diacetate (VII).

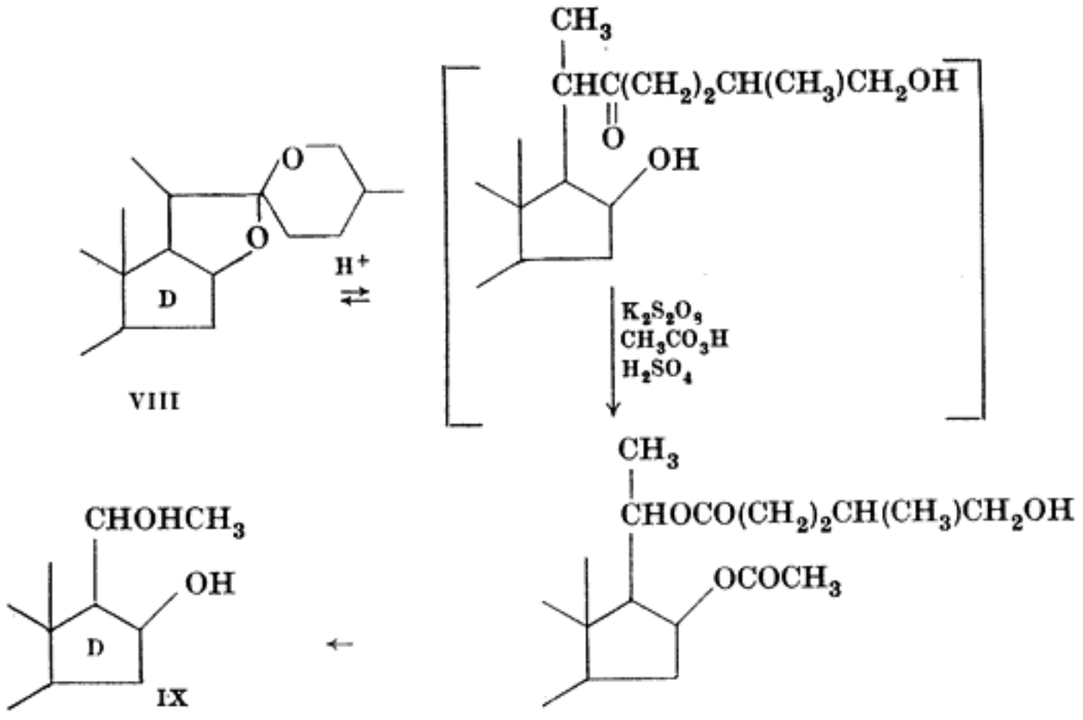


VII

This method was first applied using persulfuric acid,[24] but low yields were sometimes obtained,[25] and alternative procedures for the preparation of C–17 alcohols appeared preferable.[26] However, it has been found that perbenzoic acid and monoperphthalic acid give higher yields, particularly when acid catalysts are present.[27, 28] Also, unlike the alternative procedures, which involve ozonization or nitrosation, the reaction may be applied to unsaturated ketones such as pregnenolone.

The oxidation has been used as the key step in a degradation of sarsapogenin (VIII) to pregnan-3,16,20-triol (IX).[29]

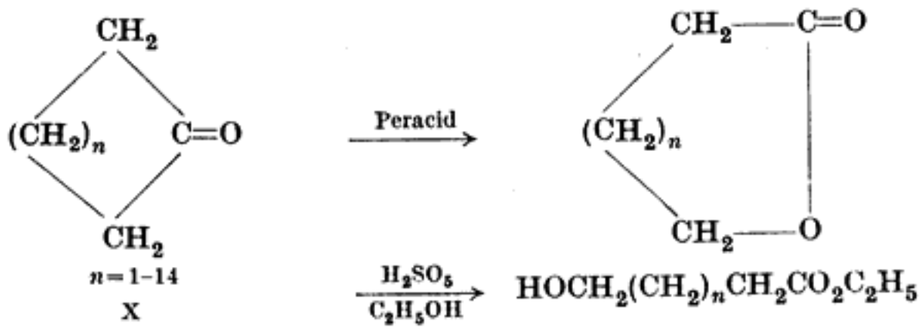
[23] Friess and Pinson, *J. Am. Chem. Soc.*, **74**, 1302 (1952).
[24] Marker and co-workers, *J. Am. Chem. Soc.*, **62**, 650, 2543, 2621, 3003 (1940).
[25] Koechlin and Reichstein, *Helv. Chim. Acta*, **27**, 549 (1944).
[26] Fieser and Fieser, *Natural Products Related to Phenanthrene*, 3rd ed., p. 400, Reinhold Publishing Corp., 1949.
[27] Sarett, *J. Am. Chem. Soc.*, **69**, 2899 (1947).
[28] Wieland and Miescher, *Helv. Chim. Acta*, **32**, 1768 (1949).
[29] Marker, Rohrmann, Crooks, Whittle, Jones, and Turner, *J. Am. Chem. Soc.*, **62**, 525 (1940).



VIII IX

The value of the Baeyer-Villiger reaction in this series is enhanced by decisive evidence that rearrangement occurs with retention of configuration.[7, 30, 31] This fact has been utilized in the preparation of 2-decalols and C–17 hydroxy steroids of definite configuration.[32]

Alicyclic Ketones. Alicyclic ketones ranging from cyclobutanone to cycloheptadecanone (X, $n = 14$)[5, 33, 34] have been oxidized under Baeyer-Villiger conditions. The reaction provides a convenient method for determining structure and for preparing relatively inaccessible lactones and hydroxy acids. When persulfuric acid or hydrogen peroxide-hydrofluoric acid[20] is used for the oxidation, polyesters of the hydroxy acids are obtained. The ethyl esters of the simple hydroxy acids are formed when ethanol is present.[35] Organic peracids give excellent yields of lactones.

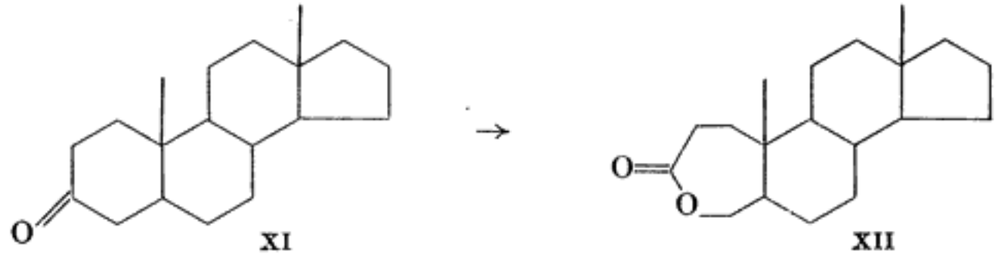


X

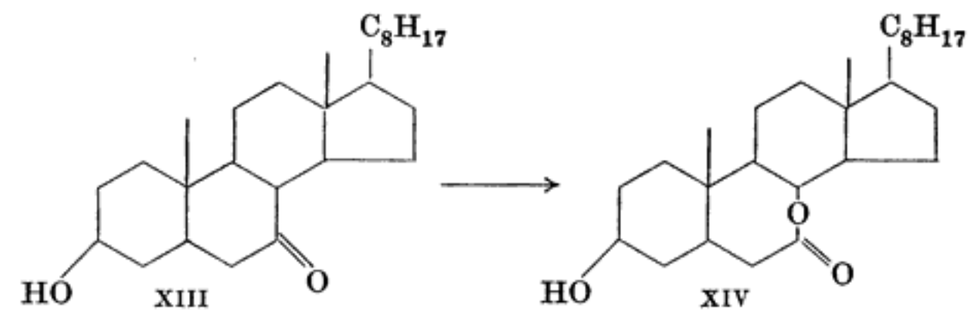
[30] Mislow and Brenner, *J. Am. Chem. Soc.*, **75**, 2319 (1953).
[31] Gallagher and Kritchevsky, *J. Am. Chem. Soc.*, **72**, 882 (1950).
[32] Dauben and Hoerger, *J. Am. Chem. Soc.*, **73**, 1505 (1951).
[33] Friess and Frankenburg, *J. Am. Chem. Soc.*, **74**, 2679 (1952).
[34] Ruzicka and Stoll, *Helv. Chim. Acta*, **11**, 1159 (1928).
[35] Robinson and Smith, *J. Chem. Soc.*, **1937**, 371.

The oxidation has also been carried out under alkaline conditions but the yields recorded are low.[36–38]

In the steroid series the procedure has been applied to compounds having carbonyl groups at C–3,[28, 39–43] C–7,[44] and C–17.[45, 46] It has been demonstrated that conditions suitable for the oxidation of such compounds do not lead to any action on C–11[27] or C–12[40] carbonyl groups, although oxidation at C–12 does occur when a large excess of peracid is used. There is evidence that oxidation of the C–3 carbonyl group of cholestan-3-one and coprostan-3-one with persulfuric acid is inhibited by the presence of bromine in the 2- or 4-positions,[47] but that is not the case when excess perbenzoic acid is employed.[28] The oxidation of androstan-3-one (XI) gives the lactone XII.[43] 7-Ketocholestan-3β-ol (XIII) is oxidized to the lactone XIV.[44]



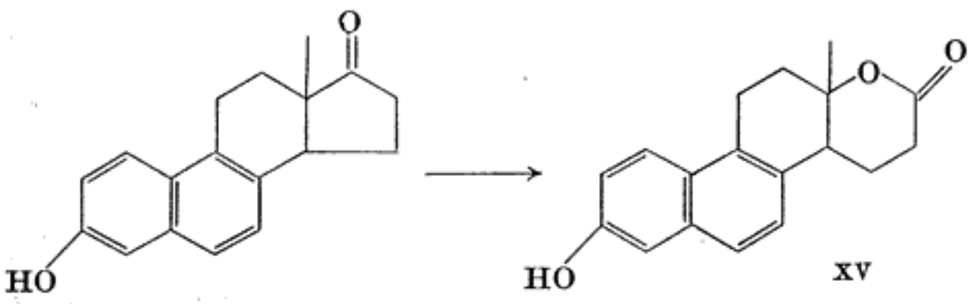
XI XII



XIII XIV

In the oxidation of 17-keto steroids there is some doubt as to which bond adjacent to the carbonyl group is broken, but the evidence available favors the formulation XV for the lactone.[46]

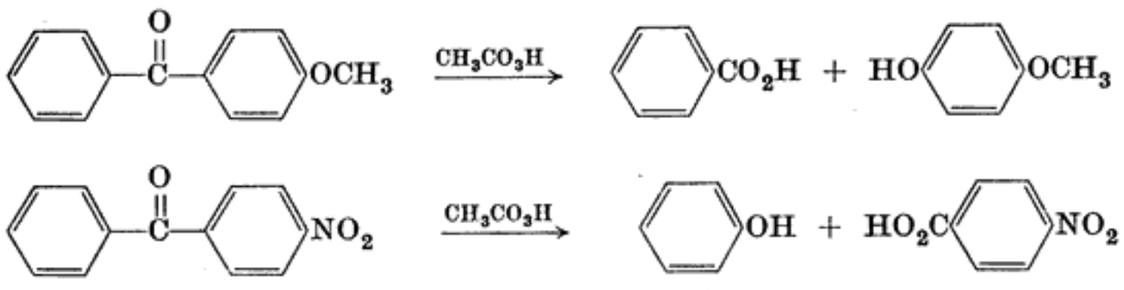
[36] Westerfield, *J. Biol. Chem.*, **143**, 177 (1942).
[37] Fling, Minard, and Fox, *J. Am. Chem. Soc.*, **69**, 2467 (1947).
[38] Heine and Jones, *J. Am. Chem. Soc.*, **73**, 1361 (1951).
[39] Gardner and Godden, *Biochem. J.*, **7**, 588 (1913).
[40] Burckhardt and Reichstein, *Helv. Chim. Acta*, **25**, 1434 (1942).
[41] Ruzicka, Prelog, and Meister, *Helv. Chim. Acta*, **28**, 1651 (1945).
[42] Salamon, *Z. physiol. Chem.*, **272**, 61 (1941).
[43] Prelog, Ruzicka, Meister, and Wieland, *Helv. Chim. Acta*, **28**, 618, 1651 (1945).
[44] Heusser, Segrè, and Plattner, *Helv. Chim. Acta*, **31**, 1183 (1948).
[45] Jacobsen, *J. Biol. Chem.*, **171**, 61 (1947).
[46] Picha, *J. Am. Chem. Soc.*, **74**, 703 (1952).
[47] Marker, *J. Am. Chem. Soc.*, **62**, 2543 (1940).



XV

Aromatic Ketones. The oxidation of diaryl ketones with peracids regularly leads to the formation of esters or their hydrolysis products. Although this reaction is of little value as a preparative procedure, it does provide a convenient means of establishing the structures of polysubstituted benzophenones and alkyl aryl ketones.[48] The method is less drastic and more specific than the degradation procedures involving alkali fusion[49] or acid hydrolysis[50] that have been applied to natural products.

In the cleavage of unsymmetrical ketones the migrating group is normally the more electron-releasing one. Substituents in the aromatic nuclei influence the course of reaction in a manner similar to that observed in normal nucleophilic aromatic substitution. Thus treatment of *p*-methoxybenzophenone with peracetic acid gives benzoic acid and hydroquinone monomethyl ether, while cleavage of *p*-nitrobenzophenone gives *p*-nitrobenzoic acid and phenol exclusively.[4]



Insufficient information is available to make it possible to predict the course of reaction of alkyl aryl ketones with certainty. Treatment with peracids and hydrogen peroxide in acid or neutral solution may lead to the migration of either the aromatic or the aliphatic group.[10] Thus, with peracetic acid, acetophenone gives a mixture of esters,[4] and cyclohexyl phenyl ketone gives esters XVI and XVII in the approximate proportion of 5 : 1.[51]

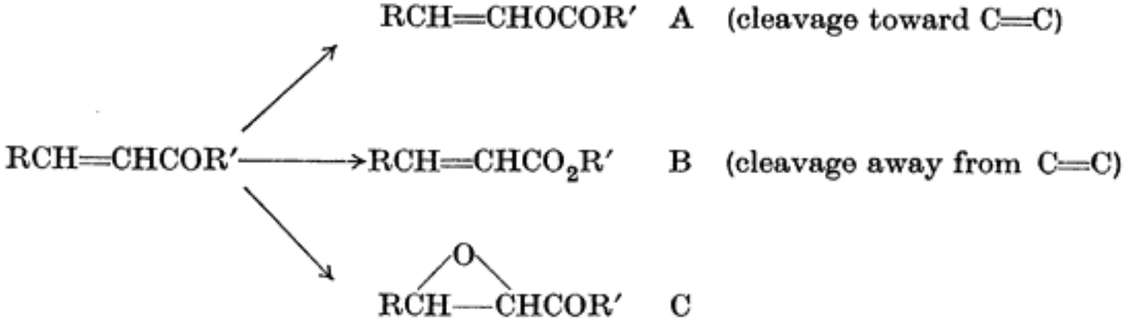
$$C_6H_5COC_6H_{11} \rightarrow \underset{\text{XVI}}{C_6H_5CO_2C_6H_{11}} + \underset{\text{XVII}}{C_6H_{11}CO_2C_6H_5}$$

[48] Ballio and Almirante, *Ann. chim. Rome*, **41**, 421 (1951) [*C. A.*, **46**, 2518 (1952)].
[49] Kostanecki, *Ber.*, **39**, 4014 (1906).
[50] Graebe and Eichengrun, *Ann.*, **269**, 320 (1892).
[51] Friess and Farnham, *J. Am. Chem. Soc.*, **72**, 5518 (1950).

However, in one study of the oxidation of *meta*- and *para*-substituted acetophenones with perbenzoic acid, acetates alone were obtained in good yields.[10]

Alkyl aryl ketones containing hydroxyl groups in the *ortho* or *para* position are converted to polyhydric phenols by hydrogen peroxide in alkaline solution. The yields are poor.[52]

α,β-Unsaturated Ketones. The application of the Baeyer-Villiger reaction to this group of compounds should lead to reaction according to either A or B. Another possibility is preferential attack at the olefinic linkage leading to an α,β-epoxyketone (C).



Although only a limited number of cases have been studied, examples of the formation of all three types of compound are available. The oxidation of benzalacetone (XVIII) with peracetic acid leads exclusively to the ester XIX.[53]

$$\underset{\text{XVIII}}{C_6H_5CH{=}CHCOCH_3} \rightarrow \underset{\text{XIX}}{C_6H_5CH{=}CHOCOCH_3}$$

An α-phenyl-α,β-unsaturated ketone (XX) gives a mixture of epoxyketone and the ester XXI.[54]

$$\underset{\text{XX}}{RCH{=}C(C_6H_5)COCH_3} \rightarrow RCH{=}\underset{\text{XXI}}{C(C_6H_5)CO_2CH_3} + \overset{O}{\diagup\!\diagdown}\!RCH{-}C(C_6H_5)COCH_3$$

Oxidation of Δ^{16}-20-ketosteroids with perbenzoic acid leads to preferential attack at the olefinic linkage. Pregna-5,6-dien-3β-ol-20-one acetate has been converted in this way to 16,17-epoxypregna-5-en-3β-ol-20-one acetate, a useful intermediate in the preparation of 17α-hydroxyprogesterone.[55]

When α,β-unsaturated ketones are treated with hydrogen peroxide in alkaline solution, epoxyketones are formed.[56–58] There is no evidence of the Baeyer-Villiger reaction occurring under these conditions.

[52] Dakin, *Am. Chem. J.*, **42**, 474 (1909).
[53] Böeseken and Soesman, *Rec. trav. chim.*, **52**, 874 (1933).
[54] Wenkert and Rubin, *Nature*, **170**, 708 (1952).
[55] Julian, Meyer, and Ryden, *J. Am. Chem. Soc.*, **72**, 367 (1950).
[56] Kohler, Richtmeyer, and Hester, *J. Am. Chem. Soc.*, **53**, 213 (1931).
[57] Fieser and co-workers, *J. Am. Chem. Soc.*, **61**, 3216 (1939); **62**, 2866 (1940).
[58] Barkley, Farrar, Knowles, and Raffelson, *J. Am. Chem. Soc.*, **75**, 4110 (1953).

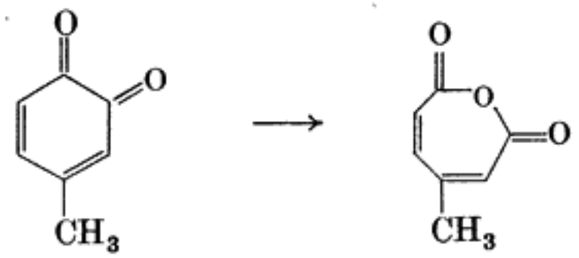
Polycarbonyl Compounds. α-Diketones and α-keto acids react readily with Baeyer-Villiger reagents.[59–64] In inert solvents anhydrides are formed,[65–67] while in alkaline or acidic media simple carboxylic acids are generally produced in good yields. It would appear from some comparisons of conditions that higher yields are obtained when the oxidations are conducted in alkaline solution.[68]

The oxidation has been used in establishing structure and in the preparation of relatively inaccessible carboxylic acids. As typical examples, 9,10-diketostearic acid is converted quantitatively to azelaic and pelargonic acid,[61]

$$CH_3(CH_2)_7COCO(CH_2)_7CO_2H + CH_3CO_3H \rightarrow CH_3(CH_2)_7CO_2H + HO_2C(CH_2)_7CO_2H$$

and phenanthraquinone forms diphenic acid.[69, 70]

Unsaturated α-diketones react in a similar manner. Treatment of 4-methyl-*o*-benzoquinone (XXII) with monoperphthalic acid gives β-methylmuconic anhydride XXIII.[65]



XXII XXIII

Dicinnamylidenebiacetyl (XXIV) is oxidized to the anhydride XXV,[65]

$$C_6H_5(CH{=}CH)_2COCO(CH{=}CH)_2C_6H_5 \rightarrow$$

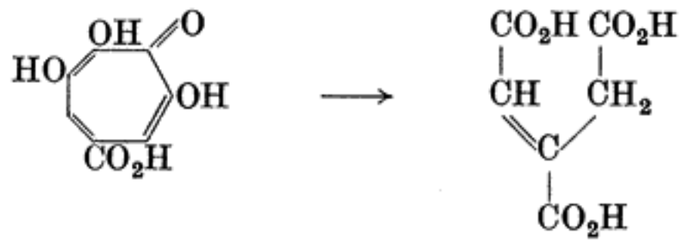
XXIV

$$C_6H_5(CH{=}CH)_2CO_2CO(CH{=}CH)_2C_6H_5$$

XXV

[59] French and Sears, *J. Am. Chem. Soc.*, **70**, 1279 (1948).
[60] Holleman, *Rec. trav. chim.*, **23**, 170 (1904).
[61] Böeseken and Sloof, *Rec. trav. chim.*, **49**, 91 (1930).
[62] Reissert, *Ber.*, **30**, 1041 (1897).
[63] Weitz and Scheffer, *Ber.*, **54**, 2327 (1921).
[64] Bjorklund and Hatcher, *Trans. Roy. Soc. Can.*, (III), **44**, 25 (1950) [*C. A.*, **45**, 7951 (1951)].
[65] Karrer, Schwyzer, and Neuwirth, *Helv. Chim. Acta*, **31**, 1210 (1948).
[66] Karrer, Cochand, and Neuss, *Helv. Chim. Acta*, **29**, 1836 (1946).
[67] Karrer and Hohl, *Helv. Chim. Acta*, **32**, 1932 (1949).
[68] Meyer, *Helv. Chim. Acta*, **30**, 1976 (1947).
[69] Linstead and Walpole, *J. Chem. Soc.*, **1939**, 855.
[70] Perkin, *Proc. Chem. Soc.*, **23**, 166 (1907).

and puberulic acid (XXVI), presumably reacting through the keto form, is oxidized to aconitic acid (XXVII),[71]



XXVI XXVII

The oxidation of α-diketones normally involves cleavage between the carbonyl groups. However, it has been shown that the reaction of 2,2′,4,4′-tetranitrobenzil with alkaline hydrogen peroxide gives 2,4-dinitrophenol and not 2,4-dinitrobenzoic acid which is formed in an acidic medium.[72]

The oxidation of 1,3-diketones and β-keto acids with peracids does not follow the normal pattern of the Baeyer-Villiger reaction. Treatment of dibenzoylmethane derivatives with perbenzoic acid leads to the formation of the corresponding dibenzoylcarbinols.[73–76]

$$C_6H_5COCH_2COC_6H_5 \rightarrow C_6H_5COCH(OH)COC_6H_5$$

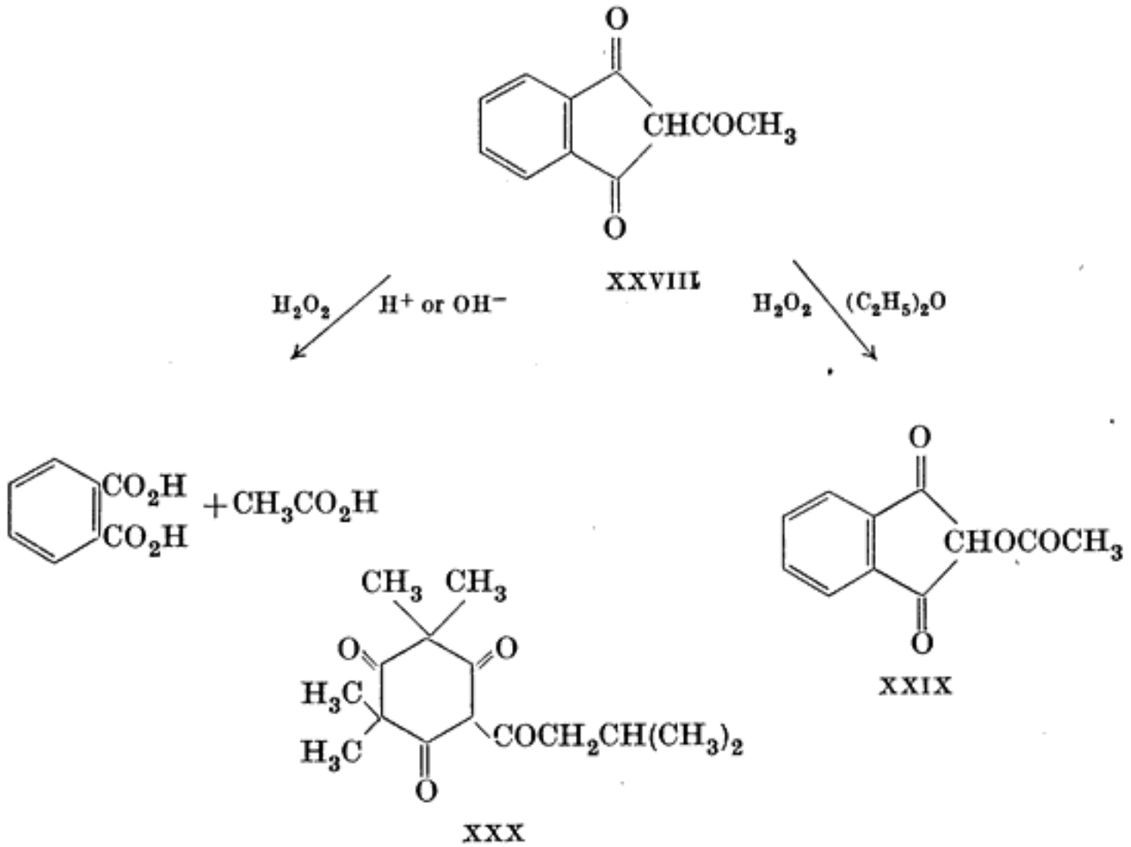
In an earlier study[77] it was found that an equimolecular amount of peracetic acid oxidized 1,3-diketones or β-keto acids to an acid and an alcohol. With excess peracetic acid a mixture of acids is formed. The first reaction was interpreted as involving migration of the group R′ lying between the carbonyl groups.

$$RCOCH(R')COR'' + CH_3CO_3H \rightarrow RR'CHOH + R''COCO_2H$$

$$R{=}CH_3,\ C_2H_5,\ C_5H_{11};\ R'{=}H,\ CH_3,\ C_6H_5CH_2;\ R''{=}CH_3,\ OC_2H_5$$

When β-triketones such as 2-acetylindan-1,3-dione (XXVIII) are treated with hydrogen peroxide in diethyl ether there is preferential oxidation of the acyl side chain leading to the formation of an ester (XXIX).[78] In acidic or alkaline media, hydrogen peroxide oxidizes 2-acetylindan-1,3-dione to a mixture of acetic and phthalic acids.

[71] Corbett, Hassall, Johnson, and Todd, *Chemistry & Industry*, **1949**, 626.
[72] Blatt and Rytina, *J. Am. Chem. Soc.*, **72**, 403 (1950).
[73] Blatt and Hawkins, *J. Am. Chem. Soc.*, **58**, 81 (1936).
[74] Karrer, Albers-Schonberg, and Kebrle, *Helv. Chim. Acta*, **35**, 1498 (1952).
[75] Karrer, Kebrle, and Thakkar, *Helv. Chim. Acta*, **33**, 1711 (1950).
[76] Karrer, Kebrle, and Albers-Schonberg, *Helv. Chim. Acta*, **34**, 1014 (1951).
[77] Böeseken and Jacobs, *Rec. trav. chim.*, **55**, 804 (1936).
[78] Hassall, *J. Chem. Soc.*, **1948**, 50.



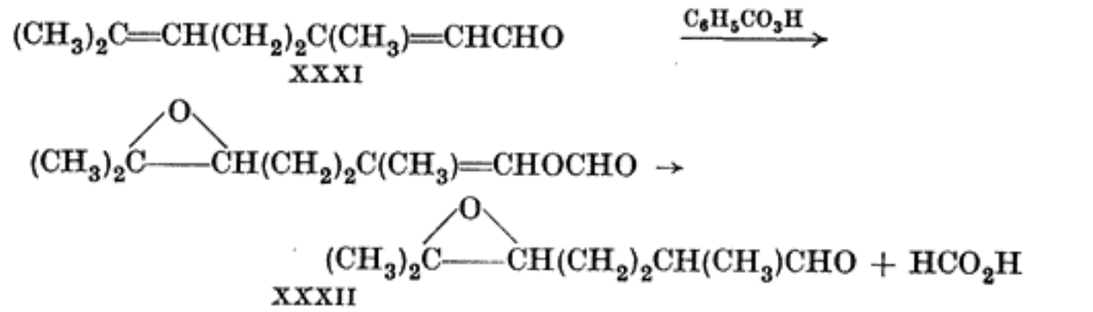
The Baeyer-Villiger reaction has been used in the elucidation of the structure of the natural product leptospermone (XXX).[79]

Aldehydes. Peracids generally convert both aliphatic and aromatic aldehydes to carboxylic acids.[80–83] Hydrogen peroxide reacts with aliphatic aldehydes in neutral media to give hydroxyhydroperoxides.[84, 11] It is significant, however, that such peroxides rearrange readily on heating to give a mixture of the corresponding carboxylic acid and the formate of the next lower alcohol. This behavior suggests that the oxidation of aldehydes with peroxides normally follows the Baeyer-Villiger pattern.

$$CH_3(CH_2)_5CHO + H_2O_2 \rightarrow CH_3(CH_2)_5CH(OH)O_2H \xrightarrow{\text{Heat}} CH_3(CH_2)_5OCHO + CH_3(CH_2)_5CO_2H$$

The oxidation of citral (XXXI) to the lower aldehyde XXXII is an example of a similar course of reaction.[85]

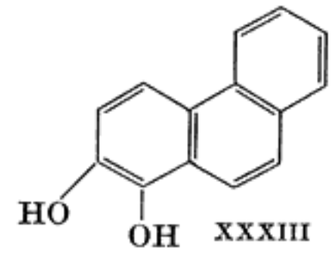
[79] Briggs, Hassall, and Short, *J. Chem. Soc.*, **1945**, 706.
[80] D'Ans and Kneip, *Ber.*, **48**, 1136 (1915).
[81] Wieland and Richter, *Ann.* **495**, 284 (1932).
[82] Lyubarskii and Kagan, *J. Phys. Chem.*, **39**, 847 (1935).
[83] Ross, Gebhart, and Gerecht, *J. Am. Chem. Soc.*, **67**, 1275 (1945).
[84] Rieche, *Alkylperoxyde und Ozonide*, p. 36, Steinkopf, Leipzig, 1931.
[85] Prilejaeff, *Bull. soc. chim. France*, [4] **42**, 687 (1927).



The oxidation of aliphatic aldehydes with hydrogen peroxide in acid and alkaline solution occasionally leads to the formation of hydrogen and hydrocarbons in addition to carboxylic acids.[86–89] Such reactions appear to involve a radical mechanism in addition to the normal ionic process.

Aromatic aldehydes have been oxidized with peroxides in a variety of media. In neutral or acid solution the action of peracids and hydrogen peroxide resembles that with alkyl aryl ketones under similar conditions.[90, 91] Benzaldehyde reacts with hydrogen peroxide in ether to give benzoic acid and only traces of phenol.[92] In aldehydes with electron-releasing substituents such as alkoxyl, hydroxyl, and amino[93] in the *ortho* or *para* positions, the formyl group tends to migrate, producing formates or phenols according to the conditions employed.

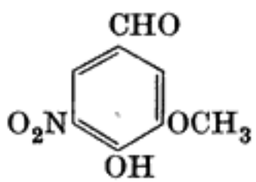
The oxidation of aromatic aldehydes in alkaline solution was first studied by Dakin,[52] who indicated that the reaction occurred only when hydroxyl groups were present in the *ortho* or *para* positions. In such cases good yields of polyhydric phenols are obtained through the replacement of formyl by hydroxyl groupings. As Table VI indicates, the Dakin procedure has been applied successfully to a variety of substituted phenolic aldehydes. It has been used for the synthesis of phenols such as morphol[94] (XXIII) which are not readily accessible by other means.



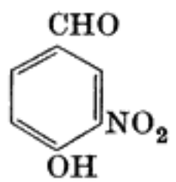
XXXIII

[86] Payne and Lemon, *J. Am. Chem. Soc.*, **63**, 226 (1941).
[87] Fry and Payne, *J. Am. Chem. Soc.*, **53**, 1973 (1931).
[88] Bezzi, *Gazz. chim. ital.*, **63**, 345 (1933).
[89] Bach and Generosov, *Ber.*, **55**, 3560 (1922).
[90] Böeseken and Group, *Rec. trav. chim.*, **58**, 528 (1939).
[91] Wacek and Bezard, *Ber.*, **74**, 845 (1941).
[92] Späth, Pailer, and Gergoley, *Ber.*, **73**, 935 (1940).
[93] Bamberger, *Ber.*, **36**, 2042 (1903).
[94] Barger, *J. Chem. Soc.*, **113**, 218 (1918).

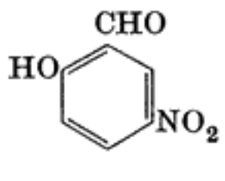
It is of interest that the aldehydes XXXIV and XXXV, in which there is a nitro group *ortho* to the hydroxyl, are not attacked, while the aldehydes XXXVI and XXXVII react in the normal way.[52] The inhibiting effect



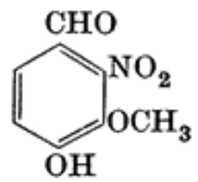
XXXIV



XXXV



XXXVI



XXXVII

is probably due to intramolecular hydrogen bonding. It has been suggested that the Dakin oxidation follows a different course from the Baeyer-Villiger reaction,[95] but this has not been substantiated.[91]

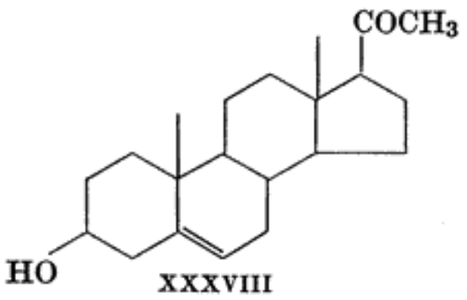
Side Reactions. Structural elements other than carbonyl groups may be attacked under the conditions used for the Baeyer-Villiger reaction. The susceptibility of olefinic linkages to oxidation by peracids is well known.[96] Aromatic hydrocarbons, such as mesitylene,[97] methylcholanthrene, and benzpyrene,[98] which are particularly sensitive to attack by electrophilic reagents, may be oxidized preferentially. The reactivity of other groupings was reviewed in 1949.[99]

There are some isolated examples of oxidation of the normal products of reaction by Baeyer-Villiger reagents. For example, phenols may react with peracids,[100–102] and demethylation of aromatic ethers may occur.[102] Catechols and hydroquinones may be oxidized through quinones[70] to carboxylic acids.[103, 104] However, if a large excess of reagent is avoided it is generally possible to obtain substantial yields of phenols from Baeyer-Villiger reactions.[48] In one example of the Dakin reaction, the oxidation of 2-hydroxy-5-methoxybenzaldehyde, the formation of an unidentified, abnormal product has been reported.[105]

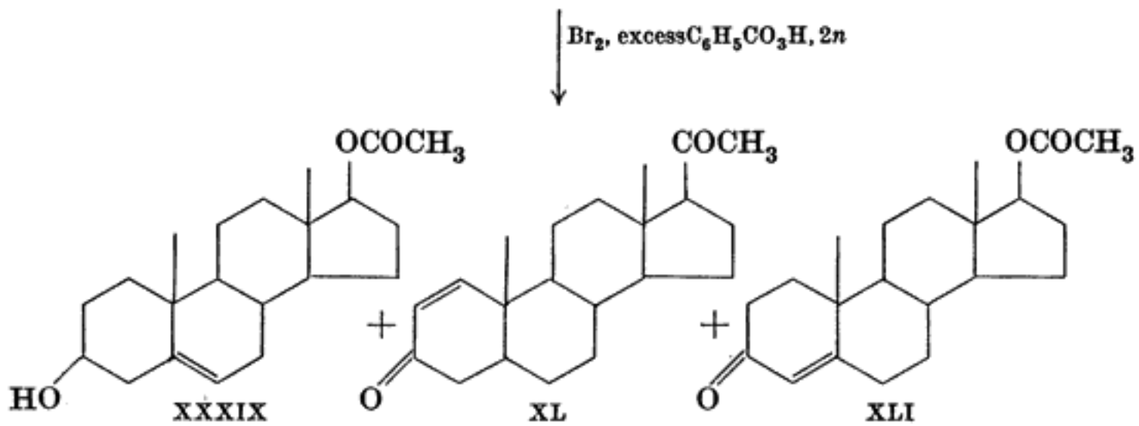
There is evidence, in two cases, of oxidation of secondary alcohols by the action of excess peracetic acid. When 1,3-diketones react with excess of this peracid, a ketone is obtained in the place of the secondary alcohol produced with an equimolar amount.[77] The steroid hydroxy ketone

[95] Wacek and Eppinger, *Ber.*, **73**, 644 (1940).
[96] Swern, *Org. Reactions*, **7**, 378 (1953).
[97] Friess and Miller, *J. Am. Chem. Soc.*, **72**, 2611 (1950).
[98] Eckhardt, *Ber.*, **73**, 13 (1940).
[99] Swern, *Chem. Revs.*, **45**, 1 (1949).
[100] Böeseken and Engelberts, *Proc. Acad. Sci. Amsterdam*, **34**, 1292 (1931) [*C. A.*, **26**, 2970 (1932)].
[101] Fernholz, *Chem. Ber.*, **84**, 110 (1951).
[102] Friess, Soloway, Morse, and Ingersoll, *J. Am. Chem. Soc.*, **74**, 1305 (1952).
[103] Wacek and Fiedler, *Monatsh.*, **80**, 170 (1949).
[104] Weitz, Schobbert, and Seibert, *Ber.*, **68**, 1163 (1935).
[105] Rosenblatt and Rosenthal, *J. Am. Chem. Soc.*, **75**, 4607 (1953).

XXXVIII is oxidized with excess peracetic acid to the diketone XL and to XLI in addition to the normal product XXXIX.[28] The rearrangement of the double bond from the β,γ to the α,β position resembles that observed in other oxidations of Δ^5-3-hydroxy steroids.[106] The oxidation of *allo*-



XXXVIII



pregnan-20-one with persulfuric acid gives, in addition to the normal product androstan-17β-ol, a significant yield of *allo*pregnan-21-ol-20-one.[47] This arises from the action of the peracid on the enolic form of the C–20 keto group.[18]

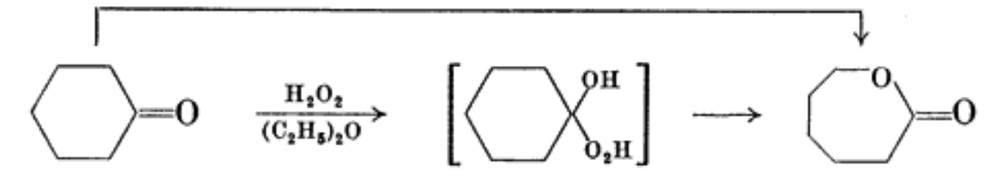
SELECTION OF EXPERIMENTAL CONDITIONS

Peroxides. Hydrogen peroxide, permono- and perdi-sulfuric acid, peracetic acid, perbenzoic acid, and monoperphthalic acid have all been used as reagents in the Baeyer-Villiger reaction. Although there is little precise information on the relative efficiencies of these peroxides, there is sufficient evidence to permit some general conclusions.

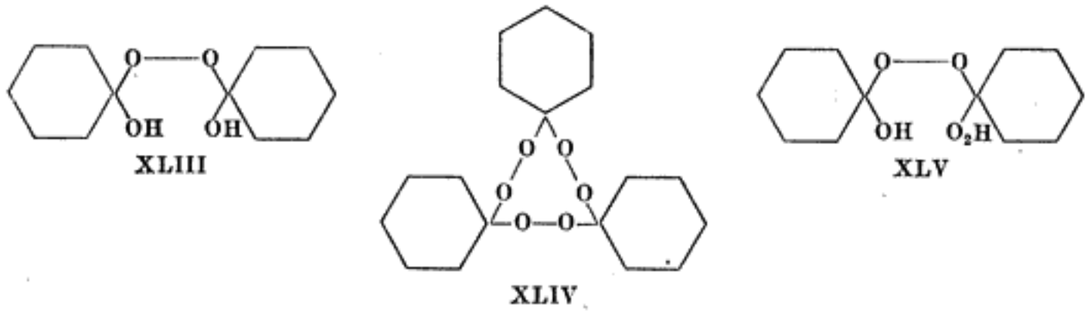
Hydrogen peroxide in dilute acid or in neutral solution sometimes converts carbonyl compounds to normal Baeyer-Villiger oxidation products, but more frequently hydroxyhydroperoxides and their condensation products are formed. The simple and condensed peroxides XLII–XLV are produced by the action of hydrogen peroxide in diethyl ether on cyclohexanone.[107, 15] Similar compounds are formed from aliphatic aldehydes[11]

[106] Djerassi, *Org. Reactions*, **6**, 212 (1951).
[107] Milas and Panagiotakos, *J. Am. Chem. Soc.*, **61**, 2430 (1939).

and fluorenone[14] under these conditions, although normal Baeyer-Villiger oxidation products are obtained without difficulty when peracids are used.



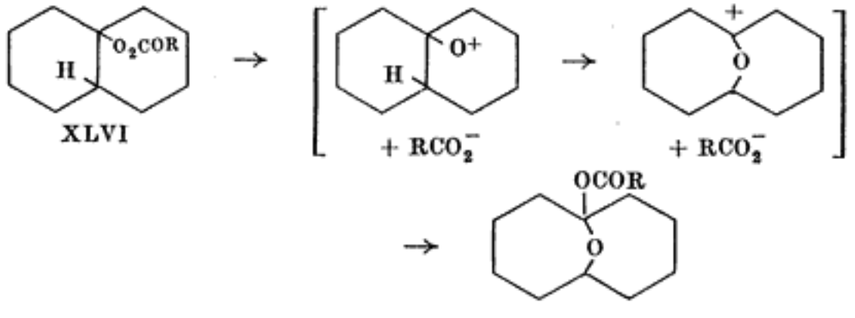
XLII



XLIII XLIV XLV

From these observations and the fact that the peroxides of cyclohexanone, fluorenone, and aliphatic aldehydes are converted by heating or by treatment with acids to the Baeyer-Villiger reaction products, it appears that hydrogen peroxide in ether or dilute acid is less effective since it does not favor the dissociation and rearrangement steps postulated for the Baeyer-Villiger reaction (p. 75).

In the related rearrangement of esters of the hydroperoxide formed from decahydronaphthalene (XLVI),[2] the dissociation step is influenced both by hydrogen-ion catalysis and by the nature of the acyl group RCO. The



XLVI

acetate and benzoate rearrange readily on warming. The *p*-nitrobenzoate rearranges more readily than the benzoate, and all attempts to prepare the trichloracetate lead to the rearrangement product. By analogy, it may be expected that the Baeyer-Villiger reaction is favored by conditions leading to the formation of peroxide esters of relatively strong acids. There is little evidence on this point, but the fact that the organic peracids

have proved more generally useful than hydrogen peroxide is in agreement with this view. The more limited applicability of the persulfuric acids is to be attributed in part to the fact that their use in aqueous solution favors the formation of peroxides. Though persulfuric acids and their salts have been used successfully in non-aqueous media, organic peracids are more convenient.

Hydrogen peroxide in alkaline solution differs in reactivity from other Baeyer-Villiger reagents. In the Dakin reaction and the cleavage of α-diketones, alkaline conditions are to be preferred. With α,β-unsaturated ketones, however, these conditions lead exclusively to epoxyketones rather than Baeyer-Villiger reaction products. There has been a useful study of the kinetic course of the oxidation of mesityl oxide and of ethylideneacetone by hydrogen peroxide in an alkaline medium.[107a] It would be desirable to obtain further information on the course and kinetics of reactions involving alkaline hydrogen peroxide.

In all peroxide oxidations of new compounds the possibility of reactions occurring with explosive violence must be considered. Trial experiments should be carried out using small quantities of material. Large excesses of reagents should be avoided, and if significant quantities of unconsumed peroxides remain at the end of the reaction they should be destroyed by reducing agents such as sodium bisulfite or ferrous sulfate before isolation of the products is attempted.

It is generally possible to follow the course of the Baeyer-Villiger reaction by estimating the active oxygen at intervals. Blank determinations should be carried out, particularly when long reaction times are involved, as the reagents may decompose under the conditions of the experiment. Information on conditions influencing the stability of peroxides is included in reviews on the general properties of hydrogen peroxide[108–110] and peracids.[99] In addition to temperature and *p*H, such factors as intensity of illumination, solvent polarity, and trace-metal impurities may play an important role.[111–113]

The following procedures are convenient for the preparation of the peroxides used in the Baeyer-Villiger reaction. Further information on methods of preparation of organic peracids is included in reviews,[96, 99, 114] and also procedures for the analysis of peroxides have been summarized.[115]

[107a] Bunton and Minkoff, *J. Chem. Soc.*, **1949**, 665.
[108] Shanley and Greenspan, *Ind. Eng. Chem.*, **39**, 1536 (1947).
[109] Medard, *Compt. rend.*, **222**, 1491 (1946).
[110] Schumb, *Ind. Eng. Chem.*, **41**, 992 (1949).
[111] Böeseken and Blumberger, *Rec. trav. chim.*, **44**, 90 (1925).
[112] Calderwood and Lane, *J. Phys. Chem.*, **45**, 108 (1941).
[113] Meerwein, Ogait, Prang, and Serini, *J. prakt. Chem.*, **113**, 9 (1926).
[114] Criegee, *Fortschr. chem. Forsch.*, **1**, 508 (1950).
[115] Swern, *Org. Reactions*, **7**, 392 (1953).

Hydrogen Peroxide. In alkaline solution, hydrogen peroxide decomposes relatively rapidly and is particularly sensitive to impurities.[108] These facts must be taken into consideration to ensure that a sufficient excess of reagent is available. The majority of Baeyer-Villiger oxidations involving alkaline hydrogen peroxide employ dilute sodium hydroxide in slight excess of the amount required to keep the reactants and products in solution. Ammonium hydroxide[52] and potassium bicarbonate[68] have also been used, and pyridine has been added in reactions in which the sodium salt of the starting material is relatively insoluble in water.[79, 94]

Hydrogen peroxide in ether is conveniently prepared by shaking 50 g. of 30% hydrogen peroxide with five 100-ml. portions of diethyl ether. The ether extract is dried first with sodium sulfate and then with calcium chloride. It contains approximately 2% hydrogen peroxide. A more concentrated solution (4–6%) may be obtained by evaporation of ether from the dilute solution at room temperature under reduced pressure.[92] The concentration of hydrogen peroxide may be determined iodimetrically. Ceric sulfate is used for the titration of hydrogen peroxide when aldehydes are present.[86, 116]

Hydrogen peroxide has also been used in acetone,[95] in formic acid-chloroform,[117] and in acetic acid.[118] It has been shown in the oxidation of androsterone acetate that a dilute solution of peracetic acid in glacial acetic acid is preferable to hydrogen peroxide in acetic acid.[119]

Persulfuric Acid. Baeyer and Villiger's "dry reagent" is prepared by mixing 10 g. of potassium persulfate with 11 g. of concentrated sulfuric acid in a mortar, adding 30 g. of potassium sulfate, and grinding the mixture to a fine powder.[1] This reagent is stable in the absence of moisture.

Oxidations have been carried out using suspensions of the dry reagent[1] or solutions of persulfuric acid in glacial acetic acid,[47] in concentrated and dilute sulfuric acid, in petroleum ether,[34] and in ethanol-sulfuric acid.[35] Methods for the estimation of permono- and perdi-sulfuric acid have been described.[120, 121]

Perbenzoic Acid. Details of the preparation of this acid are given in *Organic Reactions*.[122] A product of 99.7% purity is prepared by vacuum sublimation of crude material at 40°.[123]

[116] Willard and Young, *J. Am. Chem. Soc.*, **55**, 3260 (1933).
[117] Prelog and Kocor, *Helv. Chim. Acta*, **31**, 237 (1948).
[118] Mannich, *Ber.*, **74**, 1007 (1941).
[119] Levy and Jacobsen, *J. Biol. Chem.*, **171**, 71 (1947).
[120] D'Ans and Friederich, *Ber.*, **43**, 1880 (1910).
[121] Rius and Zulueta, *Anales real soc. españ. fis. y quim.*, **44B**, 923 (1948) [*C. A.*, **43**, 2121 (1949)].
[122] Swern, *Org. Reactions*, **7**, 394 (1953).
[123] D'Ans, Mattner, and Busse, *Angew. Chem.*, **65**, 57 (1953).

In Baeyer-Villiger oxidations perbenzoic acid is normally used in chloroform solution. Such solutions are fairly stable in the dark at low temperatures. A chloroform solution obtained from a typical *Organic Syntheses* preparation[124] (approximately 8% perbenzoic acid) lost 5.3% active oxygen on standing for twenty-one days at 2° in the dark. In five days at room temperature there was a loss of 38%.

Monoperphthalic Acid. The preparation of this acid is discussed in *Organic Reactions*.[125] Monoperphthalic acid is somewhat more stable than perbenzoic acid. At 10–15° it decomposes at the rate of approximately 2% per day. The insolubility of phthalic acid in chloroform is often an advantage in working up reaction mixtures; this property has been utilized where the products of peracid oxidation are decomposed by water.[126]

Peracetic Acid. Details of the preparation and estimation of this acid are given in *Organic Reactions*.[115, 125] Solutions containing approximately 40% peracetic acid are commercially available.[127]

Peracetic acid loses active oxygen relatively slowly. A 45% solution retains 75% of its activity after seven weeks at room temperature.[128] More stable solutions may be obtained by the addition of stabilizers or by distillation under reduced pressure.[129] The latter procedure is hazardous and it is not recommended. Peracetic acid explodes violently on heating at 110°.[130]

Solvents and Catalysts. As the tables indicate, Baeyer-Villiger reactions may be carried out using a variety of solvents. Many common organic solvents are inert under the conditions of reaction. The choice of a particular solvent is determined largely by the solubilities of the reactants and products. Rate studies have shown that reaction is favored by polar solvents,[23] but this fact has apparently not played an important role in the choice of media.

There is ample evidence that the oxidations are susceptible to catalysis by acids.[4, 5, 91, 131] Solutions containing high concentrations of sulfuric acid and hydrofluoric acid[20] may be employed with advantage. Perchloric acid,[6] sulfuric acid,[4, 29] and toluenesulfonic acid[28, 91, 119] have been used in catalytic amounts in oxidations involving peracetic and perbenzoic acids, and this may have a marked effect in reducing reaction times. As

[124] Braun, *Org. Syntheses, Coll. Vol.* 1, 431, 2nd ed., 1941.
[125] Swern, *Org. Reactions*, **7**, 395 (1953).
[126] Böhme, *Ber.*, **70**, 379 (1937).
[127] Buffalo Electrochemical Co., *Peracetic Acid Data Sheet*, I (1947).
[128] Greenspan, *J. Am. Chem. Soc.*, **68**, 907 (1946).
[129] Böeseken, Cohen, and Kip, *Rec. trav. chim.*, **55**, 815 (1936).
[130] D'Ans and Frey, *Ber.*, **45**, 1845 (1912).
[131] Dilthey, Quint, and Dierichs, *J. prakt. Chem.*, [2] **151**, 25 (1938).

a typical example, benzophenone is oxidized by peracetic acid in glacial acetic acid to phenyl acetate in 44% yield in one hundred and ninety-two hours, but when concentrated sulfuric acid (25%) is added 82% conversion occurs in thirty minutes.[4]

The oxidation of carbonyl compounds with peroxides in the presence of metal catalysts[132, 133] does not appear to follow the same course as the Baeyer-Villiger reaction.

Temperature and Time. A wide range of temperatures has been employed in Baeyer-Villiger oxidations. In some earlier applications of the reaction the carbonyl compounds were heated under reflux with peroxides in relatively high-boiling solvents. This is not to be recommended as a general procedure. Temperatures above 45° normally lead to excessive decomposition of peroxides, and under such conditions a large excess of reagent is required to replace the loss and may lead to oxidation of the normal products. There are exceptional cases involving the oxidation of aromatic aldehydes and ketones in which higher reaction temperatures have been used successfully, but in these oxidations short reaction times are involved.[48, 94] The reaction is normally carried out at a temperature of 10–40°. Lower temperatures may lead to excessively long reaction times and to reduced yields.[35]

When oxidations are carried out with organic peracids or hydrogen peroxide in neutral media, reaction times may vary from several hours to several weeks, according to the molecular species. As a typical example, oxidation of 3-ketosteroids with perbenzoic acid in chloroform is complete in sixteen hours at 16°, although under the same conditions 20-ketosteroids require seven to ten days for cleavage.[27]

In general, relatively short reaction times are required when oxidations are carried out in alkaline or strongly acidic media.

EXPERIMENTAL PROCEDURES

The following examples illustrate typical procedures for the Baeyer-Villiger reaction.

Catechol (Dakin modification using hydrogen peroxide and sodium hydroxide solution). Detailed directions for the preparation of catechol from salicylaldehyde (69–73%)[134] and for a similar preparation of 3-methoxycatechol[135] are given in *Organic Syntheses*.

3,4-Dihydroxyphenanthrene (Dakin modification using alkaline hydrogen peroxide and pyridine).[94] A solution of 1.11 g. of 3-hydroxy-4-formylphenanthrene (5 millimoles) in 10 ml. of pyridine is placed in a

[132] Treibs, *Ber.*, **72**, 1194 (1939).
[133] Milas, *J. Am. Chem. Soc.*, **59**, 2342 (1937).
[134] Dakin, *Org. Syntheses, Coll. Vol.* 1, 149, 2nd ed., 1941.
[135] Surrey, *Org. Syntheses*, **26**, 90 (1946).

25-ml. flask equipped with a dropping funnel and an exit tube. After the air has been displaced with hydrogen, 0.55 ml. of 30.8% hydrogen peroxide (50 millimoles) and 0.45 ml. of 12.5 *N* potassium hydroxide (5.6 millimoles) are added. The addition of potassium hydroxide causes a considerable rise in temperature. The solution is allowed to boil for a few seconds. It is then cooled, acidified with excess hydrochloric acid, and extracted with diethyl ether. The ether solution is washed with dilute hydrochloric acid to remove pyridine, dried, and evaporated. The crude residue (1.05 g.) is recrystallized from benzene and petroleum ether to yield 0.83 g. (80%) of pure 3,4-dihydroxyphenanthrene, m.p. 142–3°.

Phenyl *p*-Nitrobenzoate (Oxidation of a diaryl ketone using peracetic acid with sulfuric acid as catalyst).[4] A solution of 4.54 g. of *p*-nitrobenzophenone (20 millimoles) in a mixture of 50 ml. of glacial acetic acid and 30 ml. of concentrated sulfuric acid is treated with external cooling with 8 ml. of 40% peracetic acid (40 millimoles). After thirty minutes at room temperature the mixture is neutralized with sodium carbonate solution and extracted with diethyl ether. The dried ether extract yields on evaporation 4.6 g. (95%) of phenyl *p*-nitrobenzoate, m.p. 128–130°.

Etiocholan-3α,12α,17β-triol (Oxidation of a 20-keto steroid using perbenzoic acid with sulfuric acid as catalyst).[28] Ninety grams of 3α,12α-diacetoxypregnan-20-one (0.22 mole) and 44 ml. of a 10% solution of sulfuric acid in glacial acetic acid are added separately with external cooling to 440 ml. of a chloroform solution containing 68.6 g. (0.49 mole) of perbenzoic acid. The solution is allowed to stand in the dark at room temperature for ten days. After dilution with diethyl ether, the mixture is washed in turn with water, dilute sodium carbonate solution, and water. The organic layer is dried, and the solvent is evaporated. The residue is saponified by boiling for one hour with a solution of 60 g. of sodium hydroxide in 850 ml. of methanol and 50 ml. of water. After much of the methanol has been removed by distillation under reduced pressure, sufficient ether is added to keep the product in solution. The ether solution is washed with water until neutral, dried, concentrated to 600 ml., and cooled to −10° to precipitate 46.3 g. of etiocholan-3α,12α,17β-triol, m.p. 231–232°. Treatment of the concentrated mother liquor with Girard's Reagent P furnishes an additional 0.73 g. of the triol and 6.17 g. of starting material. The total yield of triol is 71%.

Diphenic Acid (Cleavage of an α-diketone using alkaline hydrogen peroxide).[136] A suspension of 1 g. of 9,10-phenanthraquinone (4.8 millimoles) in 20 ml. of 5% aqueous sodium hydroxide is mixed with 2.5 ml. of 27% hydrogen peroxide (19 millimoles) and allowed to stand with

[136] C. H. Hassall, unpublished observations.

occasional stirring at 30°. Further additions of 2.5 ml. of 27% hydrogen peroxide are made after six hours and again after an additional twelve hours. After a total of forty-eight hours the mixture is filtered from a trace of insoluble material and acidified. The precipitate of pure diphenic acid formed is collected on a filter, washed with water, and dried; the yield is 1.09 g. (94%), m.p., 229–230°.*

2-Acetoxyindan-1,3-dione (Selective oxidation of a triketomethane derivative using hydrogen peroxide in ether).[78] A solution containing 1 g. of 2-acetylindan-1,3-dione (5.3 millimoles) in 80 ml. of diethyl ether is treated with 12 ml. (18 millimoles) of 5% hydrogen peroxide in ether and allowed to stand in a closed flask at 15°. After twenty-one days the ether is evaporated. The residue is triturated with 3 ml. of water, filtered, and extracted with chloroform. The chloroform extract is filtered from a trace of phthalic acid and evaporated. The residue is crystallized twice from ethyl acetate-petroleum ether (40–60°) to give 0.70 g. (64%) of 2-acetoxyindan-1,3-dione, m.p. 96°.

Lactone $C_{21}H_{32}O_4$ from Isoandrosterone Acetate (Oxidation of a 17-keto steroid using peracetic acid with *p*-toluenesulfonic acid as catalyst).[119] A solution of 0.274 g. of isoandrosterone acetate (0.83 millimole) in 2 ml. of glacial acetic acid, 5 ml. of 9.5% peracetic acid in acetic acid (6.75 millimoles), and 25 mg. of *p*-toluenesulfonic acid are mixed and allowed to stand for twenty-three hours at 35° in the dark. The mixture is then treated with a large excess of water which precipitates 0.252 g. (88%) of the crude lactone, m.p. 156–158.5°. This product is converted by one crystallization from benzene-neohexane to the pure lactone, $C_{21}H_{32}O_4$, m.p. 158–159.5°.

TABULAR SURVEY OF THE BAEYER-VILLIGER REACTION

The following tables list all examples of the Baeyer-Villiger reaction noted in a survey of the literature available through December, 1953. The tables also include examples of oxidations of carbonyl compounds under Baeyer-Villiger conditions that have not led to the formation of the normal products of the Baeyer-Villiger reaction. The carbonyl compounds in the tables are arranged in order of increasing size of the empirical formulas. When several references are cited for a particular case, all refer to reactions under similar conditions. The yield quoted is that given in the first reference. The names of several steroids have been altered to conform with accepted conventions.

*Yields of 70%[69] and 50%[137] are obtained when hydrogen peroxide-acetic acid and chromic acid, respectively, are used as oxidizing agents.

[137] Charrier and Beretta, *Gazz. chim. ital.*, **54**, 765 (1924).

TABLE I

BAEYER-VILLIGER OXIDATION OF SATURATED ALIPHATIC KETONES

	Carbonyl Compound	Reagent*	Product	Yield, %	Reference
C_3H_6O	Acetone	H_2SO_5	Acetone peroxide	65	138, 139, 140, 64
		H_2O_2, H_2SO_4	Acetone peroxide, hydroxyacetone	—	21
C_4H_8O	Butanone	H_2O_2, H_2SO_4	Butanone peroxide, 3-hydroxybutanone	—	21, 140
C_5H_8O	Acetylcyclopropane	$C_6H_5CO_3H$	No reaction	—	141, 23
$C_5H_{10}O$	3-Pentanone	H_2O_2, H_2SO_4	3-Pentanone peroxide, 2-hydroxypentan-3-one	—	21
$C_6H_{10}O$	Acetylcyclobutane	$C_6H_5CO_3H$	Cyclobutyl acetate	58	23
$C_7H_{12}O$	Acetylcyclopentane	$C_6H_5CO_3H$	Cyclopentyl acetate	61	23
$C_8H_{14}O$	*cis*-1-Acetyl-2-methylcyclopentane	$C_6H_5CO_3H$	*cis*-2-Methylcyclopentyl acetate	66	7
	trans-1-Acetyl-2-methylcyclopentane	$C_6H_5CO_3H$	*trans*-2-Methylcyclopentyl acetate	64	7
	Acetylcyclohexane	$C_6H_5CO_3H$	Cyclohexyl acetate	67	141, 23
$C_8H_{16}O$	2-Octanone	H_2O_2, HF	*n*-Hexyl acetate	51	20
$C_9H_{16}O$	*cis*-1-Acetyl-2-methylcyclohexane	$C_6H_5CO_3H$	*cis*-2-Methylcyclohexyl acetate	63	7
	trans-1-Acetyl-2-methylcyclohexane	$C_6H_5CO_3H$	*trans*-2-Methylcyclohexyl acetate	55	7
	Acetylcycloheptane	$C_6H_5CO_3H$	Cycloheptyl acetate	69	23
$C_{10}H_{12}O$	3-Phenylbutan-2-one	$C_6H_5CO_3H$	Phenylmethylcarbinyl acetate	87	30
$C_{12}H_{20}O$	*cis-cis*-Acetyldecahydronaphthalene	$C_6H_5CO_3H$	*cis-cis*-Decahydro-2-naphthol	65	32
$C_{21}H_{34}O$	Allopregnan-20-one	$K_2S_2O_8$, CH_3CO_2H, H_2SO_4	Allopregnan-21-ol-21-one acetate, androstan-17β-ol†	30–35	47
$C_{21}H_{24}O_2$	Δ^5-Pregnen-3β-ol-20-one	$C_6H_5CO_3H$	Testosterone acetate, progesterone, Δ^5-androsten-3β,17β-diol 17-monoacetate	—	28
$C_{23}H_{34}O_3$	Δ^5-Pregnen-3β-ol-20-one acetate	Monoperphthalic acid, $CHCl_3$‡	Δ^5-Androsten-3β,17β-diol	63	28, 47
		$C_6H_5CO_3H$, $CHCl_3$, H_2SO_4	Δ^5-Androsten-3β,17β-diol	60	28
$C_{23}H_{34}O_4$	Pregnan-3α-ol-11,20-dione acetate	$C_6H_5CO_3H$	Etiocholan-3α,17β-diol-11-one diacetate†	85	27
$C_{23}H_{36}O_3$	Allopregnan-3β-ol-20-one acetate	$C_6H_5CO_3H$	Androstan-3β,17β-diol†	3	40
	Allopregnan-3α-ol-20-one acetate	$K_2S_2O_8$, CH_3CO_2H, H_2SO_4	Androstan-3α,17β-diol diacetate†	—	142
	Pregnan-3α-ol-20-one acetate	$C_6H_5CO_3H$	Etiocholan-3α,17β-diol diacetate	52	31, 47
	17-Isopregnan-3α-ol-20-one acetate	$C_6H_5CO_3H$	Etiocholan-3α,17α-diol diacetate	53	31
$C_{25}H_{38}O_5$	Pregnan-3α,12α-diol-20-one diacetate	$C_6H_5CO_3H$, $CHCl_3$, H_2SO_4§	Etiocholan-3α,12α,17β-triol	77	28, 27
$C_{28}H_{36}O_4$	Pregnan-3α-ol-11,20-dione benzoate	$C_6H_5CO_3H$	Etiocholan-3α,17β-diol-11-one 3-benzoate 17-acetate†	18	27

Note: References 138-164 are listed on p. 106.

* Where CH_3CO_3H is indicated, acetic acid is always present; where H_2SO_5 is shown, sulfuric acid is present; where $C_6H_5CO_3H$ is shown, chloroform is present.

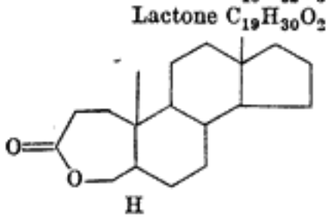
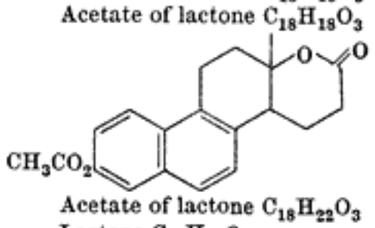
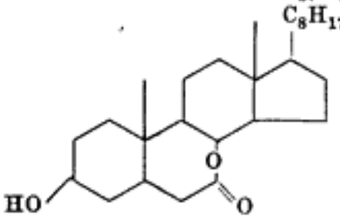
† The configuration at C–17 assigned by the author has been changed. The correction follows from the unequivocal evidence, only available after the completion of the investigation, that the Baeyer-Villiger reaction occurs with retention of configuration.

‡ A catalytic amount of *p*-$CH_3C_6H_4SO_3H$ was added.

§ Catalytic amount.

TABLE II

BAEYER-VILLIGER OXIDATION OF ALICYCLIC KETONES

	Carbonyl Compound	Reagent*	Product	Yield, %	Reference
C_4H_6O	Cyclobutanone	$C_6H_5CO_3H$	Butyrolactone	70	33
C_5H_8O	Cyclopentanone	H_2O_2, NaOH	5-Hydroxyvaleric acid lactone	18	37, 36
		H_2O_2, HF	Polyesters of 5-hydroxyvaleric acid	86–89	20
		$K_2S_2O_8$, H_2SO_4, C_2H_5OH	Ethyl 5-hydroxyvalerate	70	143, 35
		$C_6H_5CO_3H$	5-Hydroxyvaleric acid lactone	78	5
		H_2O_2, HNO_3	Cyclopentanone peroxide	—	64
$C_6H_{10}O$	Cyclohexanone	H_2O_2, HF	6-Hydroxycaproic acid lactone, polyesters of 6-hydroxycaproic acid	8, 81	20
		H_2SO_5	Polyesters of 6-hydroxycaproic acid	—	140, 69
		$K_2S_2O_8$, H_2SO_4, C_2H_5OH	Ethyl 6-hydroxycaproate	39–45	35
		H_2O_2, NaOH	6-Hydroxycaproic acid	19	38
		$C_6H_5CO_3H$	6-Hydroxycaproic acid lactone	71	5, 144
$C_7H_{12}O$	3-Methylcyclohexanone	$K_2S_2O_8$, H_2SO_4	3-Methylcyclohexanone peroxide	—	138
	Cycloheptanone	$K_2S_2O_8$, H_2SO_4, C_2H_5OH	Ethyl 7-hydroxyheptanoate	47	35, 138
		$C_6H_5CO_3H$	7-Hydroxyenanthic acid lactone	97	5
$C_8H_{14}O$	Cycloöctanone	$C_6H_5CO_3H$	8-Hydroxycaprylic acid lactone	61	33
$C_{10}H_{10}O$	α-Tetralone	H_2SO_5	4-Hydroxy-4-(*o*-hydroxyphenyl)-butyric acid lactone	—	145
$C_{10}H_{16}O$	Camphor	H_2SO_5	Campholide	22	1
$C_{10}H_{18}O$	*p*-Menthan-2-one	H_2SO_5	6-Hydroxy-3-isopropylenanthic acid lactone	40	1
	Menthone	H_2SO_5	6-Hydroxy-3,7-dimethylcaprylic acid lactone	82	140, 138
$C_{13}H_{24}O$	Cyclotridecanone	H_2SO_5	13-Hydroxytridecanoic acid lactone	41	34
$C_{14}H_{26}O$	Cyclotetradecanone	H_2SO_5	14-Hydroxymyristic acid lactone	35	34
$C_{15}H_{28}O$	Cyclopentadecanone (Exaltone)	H_2SO_5, CH_3CO_2H	15-Hydroxypentadecanoic acid lactone	47	34
		H_2O_2, H_2SO_4	Cyclopentadecanone peroxide, 15-hydroxypentadecanoic acid lactone	—	146
$C_{16}H_{30}O$	Cyclohexadecanone	H_2SO_5	16-Hydroxypalmitic acid lactone	30	34
$C_{17}H_{32}O$	Cycloheptadecanone	H_2SO_5	17-Hydroxymargaric acid lactone	53	34
$C_{18}H_{22}O_2$	Estrone	H_2O_2, NaOH	Lactone $C_{18}H_{22}O_3$	42	36
$C_{19}H_{30}O$	Androstan-3-one	$C_6H_5CO_3H$	Lactone $C_{19}H_{30}O_2$	10	43
					
$C_{19}H_{30}O_2$	Androstan-3-one-17β-ol	$C_6H_5CO_3H$	Lactone $C_{19}H_{30}O_3$	32	43
$C_{20}H_{20}O_3$	Equilenin acetate	CH_3CO_3H†	Acetate of lactone $C_{18}H_{18}O_3$	55	147
	(±)-Isoequilenin acetate	CH_3CO_3H†	Acetate of lactone $C_{18}H_{18}O_3$	69	46
					
$C_{20}H_{24}O_3$	Estrone acetate	H_2O_2, CH_3CO_2H	Acetate of lactone $C_{18}H_{22}O_3$	57–63	45
$C_{21}H_{32}O_2$	Δ⁵-Pregnen-3β-ol-20-one	$Br_2 \rightarrow C_6H_5CO_3H \rightarrow Zn$	Lactone $C_{21}H_{30}O_3$	—	63
$C_{21}H_{32}O_3$	Androsterone acetate	CH_3CO_3H†	Acetate of lactone $C_{19}H_{30}O_3$	79	119
	Isoandrosterone acetate	CH_3CO_3H†	Acetate of lactone $C_{19}H_{30}O_3$	89–92	119
$C_{23}H_{33}BrO_4$	4-Bromo-12α-acetoxypregnan-3,20-dione	$C_6H_5CO_3H$ → pyridine	Lactone $C_{23}H_{32}O_5$, lactone $C_{21}H_{30}O_5$	—	63
$C_{25}H_{38}O_3$	Δ¹¹-3-Ketocholenic acid methyl ester	$C_6H_5CO_3H$	Lactone $C_{25}H_{38}O_5$	68	148
$C_{25}H_{40}O_3$	3-Ketocholanic acid methyl ester	$C_6H_5CO_3H$	Lactone $C_{25}H_{40}O_4$	68	40
$C_{26}H_{34}O_3$	Etiocholan-17β-ol-3-one benzoate	$C_6H_5CO_3H$	Lactone $C_{26}H_{24}O_4$	95	41
$C_{27}H_{42}O_5$	3-Keto-12β-acetoxycholanic acid methyl ester	$C_6H_5CO_3H$	Lactone $C_{27}H_{42}O_6$	—	40
$C_{27}H_{44}O_2$	Cholestandione	$(NH_4)_2S_2O_8$, H_2SO_4	Lactone $C_{27}H_{44}O_4$ (?)	46	149
$C_{27}H_{46}O$	Coprostan-3-one	$C_6H_5CO_3H$	Lactone $C_{27}H_{46}O_2$	80	40, 39
	Cholestan-3-one	$C_6H_5CO_3H$	Lactone $C_{27}H_{46}O_2$	59	40
$C_{27}H_{46}O_2$	7-Ketocholestan-3β-ol	$C_6H_5CO_3H$	Lactone $C_{27}H_{46}O_3$	87	44
					
$C_{29}H_{48}O_3$	7-Ketocholestan-3β-ol acetate (benzoate or pivalate)	$C_6H_5CO_3H$	Derivatives of lactone $C_{27}H_{46}O_3$	86–100	44

Note: References 138-164 are listed on p. 106.

* Where CH_3CO_3H is indicated, acetic acid is always present; where H_2SO_5 is shown, sulfuric acid is present; where $C_6H_5CO_3H$ is shown, chloroform is present.

† A catalytic amount of p-$CH_3C_6H_4SO_3H$ was added.

TABLE III

BAEYER-VILLIGER OXIDATION OF ALIPHATIC AROMATIC, ALICYCLIC AROMATIC, AROMATIC, AND HETEROCYCLIC KETONES

Carbonyl Compound		Reagent	Product	Yield, %	Reference
C_8H_7ClO	*p*-Chloroacetophenone	$C_6H_5CO_3H$	*p*-Chlorophenyl acetate	57	10
C_8H_8O	Acetophenone	CH_3CO_3H	Phenyl acetate	33	48, 4
		$C_6H_5CO_3H$	Phenyl acetate	63	141
$C_8H_8O_2$	*o*-Hydroxyacetophenone	H_2O_2, NH_3	Catechol	—	52
	m-Hydroxyacetophenone	H_2O_2, NH_3	No reaction	—	52
	p-Hydroxyacetophenone	H_2O_2, NH_3	Hydroquinone	40–50	52
$C_8H_8O_3$	2,4-Dihydroxyacetophenone	H_2O_2, NH_3	Hydroxyhydroquinone	—	52
	2,5-Dihydroxyacetophenone	H_2O_2, NH_3	Hydroxyhydroquinone	—	52
$C_9H_7O_2Cl$	2-Methoxy-4-chloroacetophenone	CH_3CO_3H*	4-Methoxy-4-chlorophenyl acetate,	50	48
			5-chloroguaiacol	Trace	
$C_9H_{10}O$	*p*-Methylacetophenone	$C_6H_5CO_3H$	*p*-Cresyl acetate	73	10
	Propiophenone	$C_6H_5CO_3H$	Phenyl propionate	73	141
$C_9H_{10}O_2$	*p*-Hydroxypropiophenone	H_2O_2, NH_3	Hydroquinone	—	52
	o-Methoxyacetophenone	CH_3CO_3H	Guaiacol	—	48
	m-Methoxyacetophenone	$C_6H_5CO_3H$	*m*-Methoxyphenyl acetate	52	10
	p-Methoxyacetophenone	$C_6H_5CO_3H$	*p*-Methoxyphenyl acetate	66	10, 48, 90, 91
$C_9H_{10}O_3$	2-Hydroxy-4-methoxyacetophenone	H_2O_2, NH_3	1,2-Dihydroxy-4-methoxybenzene	—	150
$C_{10}H_{10}O_3$	*p*-Acetoxyacetophenone	$C_6H_5CO_3H$	Hydroquinone diacetate	80	10
$C_{10}H_{11}NO_2$	*p*-Acetaminoacetophenone	$C_6H_5CO_3H$	*p*-Acetaminophenyl acetate	80	71
$C_{10}H_{12}O_3$	2,4-Dimethoxyacetophenone	CH_3CO_3H	2,4-Dimethoxyphenol	—	48
	2,5-Dimethoxyacetophenone	CH_3CO_3H*	2,5-Dimethoxyphenyl acetate	—	48
	2,4-Dihydroxy-3,5-dimethylacetophenone (clavatol)	H_2O_2, NaOH	3-Hydroxy-2,6-dimethylbenzoquinone	30	151

$C_{11}H_{14}O$	Acetomesitylene	$C_6H_5CO_3H$	No product isolated	—	97
$C_{11}H_{14}O_4$	2,4,5-Trimethoxyacetophenone	CH_3CO_3H*	2,4,5-Trimethoxyphenyl acetate	—	48
	2,3,4-Trimethoxyacetophenone	CH_3CO_3H*	2,3,4-Trimethoxyphenyl acetate	—	48
$C_{12}H_{14}O_4$	1,3-Diacetyl-4,6-dimethoxybenzene	CH_3CO_3H*	4,6-Dimethoxyresorcinol diacetate	—	48
$C_{13}H_8O$	Fluorenone	CH_3CO_3H, H_2SO_4	2′-Hydroxybiphenyl-2-carboxylic acid lactone	—	4
		H_2O_2, $(C_2H_5)_2O$	Fluorenone peroxide,	53	14
			2′-Hydroxybiphenyl-2-carboxylic acid lactone	20	
$C_{13}H_8N_2O_5$	*o,p*′-Dinitrobenzophenone	H_2SO_5, $(CH_3CO)_2O$	2′-Hydroxybiphenyl-2-carboxylic acid lactone	96	14
	p,p′Dinitrobenzophenone	CH_3CO_3H, H_2SO_4	No reaction	—	4
$C_{13}H_9BrO$	*p*-Bromobenzophenone	CH_3CO_3H, H_2SO_4	*p*-Nitrophenol, *p*-nitrobenzoic acid	54, 82	4
$C_{13}H_9ClO$	*p*-Chlorobenzophenone	CH_3CO_3H, H_2SO_4	Phenyl *p*-bromobenzoate	60	4
		CH_3CO_2H, H_2SO_4	Phenyl *p*-chlorobenzoate, phenol, *p*-chloro-	77	4
$C_{13}H_9NO_3$	*p*-Nitrobenzophenone		benzoic acid		
$C_{13}H_{10}O$	Benzophenone	CH_3CO_3H, H_2SO_4	Phenyl *p*-nitrobenzoate	95	4, 131
$C_{13}H_{12}NO$	*p*-Aminobenzophenone	H_2SO_5, $(CH_3CO)_2O$	Phenyl benzoate	Quantitative	140, 4
$C_{13}H_{16}O$	Phenyl cyclohexyl ketone	CH_3CO_3H, H_2SO_4	Phenyl *p*-aminobenzoate	38	4
		CH_3CO_3H	Cyclohexanol, benzoic acid, phenol, hexa-	6, 33, 5, 5	4
$C_{13}H_{16}O_5$	1,3-Diacetyl-4,5,6-trimethoxybenzene		hydrobenzoic acid		
	1,3-Diacetyl-2,4,5-trimethoxybenzene	$C_6H_5CO_3H$	Cyclohexyl benzoate, phenyl hexahydrobenzoate	71, 15	51
$C_{14}H_{11}NO_2$	3-Phenyldioxindole	CH_3CO_3H*	4,5,6-Trimethoxyresorcinol diacetate	—	48
$C_{14}H_{12}O$	*p*-Methylbenzophenone	CH_3CO_3H*	2,4,5-Trimethoxyresorcinol diacetate	—	48
$C_{14}H_{12}O_2$	*p*-Methoxybenzophenone	H_2O_2, NaOH	*o*-Aminobenzophenone	—	152
$C_{15}H_{13}NO_2$	3-(*o*-Tolyl)dioxindole	CH_3CO_3H	*p*-Cresyl benzoate	14	4
	3-(*m*-Tolyl)dioxindole	CH_3CO_3H, H_2SO_4	*p*-Methoxyphenyl benzoate	96	4
	3-(*p*-Tolyl)dioxindole	H_2O_2, NaOH	*o*-Methyl-*o*′-aminobenzophenone	—	152
$C_{15}H_{13}NO_3$	3-(*o*-Methoxyphenyl)dioxindole	H_2O_2, NaOH	*m*-Toluic acid	—	152
	3-(*m*-Methoxyphenyl)dioxindole	H_2O_2, NaOH	*p*-Methyl-*o*′-aminobenzophenone	—	152
	3-(*p*-Methoxyphenyl)dioxindole	H_2O_2, NaOH	*o*-Methoxy-*o*′-aminobenzophenone	—	152
$C_{16}H_{16}O$	Phenyl mesityl ketone	H_2O_2, NaOH	*m*-Toluic acid	—	152
		H_2O_2, NaOH	*p*-Methoxy-*o*′-aminobenzophenone	—	152
		CH_3CO_3H, H_2SO_4	Benzoic acid	10	4

Note: References 138-164 are listed on p. 106.

* A catalytic amount of p-$CH_3C_6H_4SO_3H$ was added.

TABLE IV

BAEYER-VILLIGER OXIDATION OF α,β-UNSATURATED CARBONYL COMPOUNDS

	Carbonyl Compound	Reagent	Product	Yield, %	Reference
$C_6H_4O_2$	Benzoquinone	H_2O_2, NaOH	*cis*-Ethylene oxide dicarboxylic acid	53–6	104
$C_6H_{10}O$	Mesityl oxide	H_2O_2, NaOH	1,1-Dimethyl-2-acetylethylene oxide	—	63
$C_{10}H_6O_2$	α-Naphthoquinone	H_2O_2, NaOH	α-Naphthoquinone oxide	—	104
$C_{10}H_{10}O$	Benzalacetone	CH_3CO_3H	Enol acetate of phenylacetaldehyde	38	153, 53
		H_2O_2, NaOH	1-Phenyl-2-acetylethylene oxide	70	63, 56, 153
$C_{10}H_{16}O$	Citral	$C_6H_5CO_3H$	Enol formate of 2,6-dimethyl-5,6-epoxyheptaldehyde	—	85
$C_{11}H_8O_2$	2-Methyl-1,4-naphthoquinone	H_2O_2, NaOH	2-Methyl-1,4-naphthoquinone oxide	67	57
$C_{11}H_{12}O$	Methyl β-methylstyryl ketone	CH_3CO_3H	Enol acetate of methyl benzyl ketone	—	77
	Ethyl styryl ketone	CH_3CO_3H	Enol propionate of phenylacetaldehyde	69	77
$C_{15}H_{12}O$	Benzalacetophenone	H_2O_2, NaOH	1-Phenyl-2-benzoylethylene oxide	89	63
$C_{20}H_{24}O_3$	(±)-11-Keto-Δ^{16}-21-norprogesterone	H_2O_2, NaOH	(±)-11-Keto-16α,17α-epoxy-21-norprogesterone	—	58
$C_{21}H_{14}O$	10-Benzalanthrone	H_2O_2, NaOH	10,11-Epoxybenzalanthrone	—	63
$C_{21}H_{30}O_2$	Progesterone	$K_2S_2O_8$, CH_3CO_2H, H_2SO_4	Lactone $C_{20}H_{30}O_3$	43	42, 27
$C_{23}H_{19}NO$	2-Dimethylamino-10-benzalanthrone	H_2O_2, NaOH	2-Dimethylaminoanthraquinone, benzoic acid	—	63
$C_{23}H_{33}O_3$	Pregna-5,16-dien-3β-ol-20-one acetate	$C_6H_5CO_3H$	16,17-Epoxypregna-5-en-3β-ol-20-one acetate	56	55
$C_{25}H_{36}O_3$	Methyl $\Delta^{4,11}$-3-ketocholadienate	$C_6H_5CO_3H$	Methyl Δ^4-11,12-epoxy-3-ketocholenate	21	148
$C_{27}H_{44}O$	Δ^4-Cholesten-3-one	$K_2S_2O_8$, CH_3CO_2H, H_2SO_4	Lactone $C_{26}H_{44}O_2$	68	42

Note: References 138-164 are listed on p. 106.

TABLE V

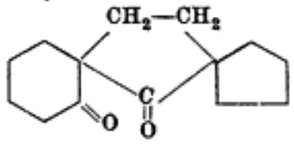
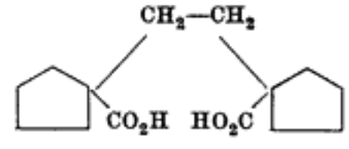
BAEYER-VILLIGER OXIDATION OF POLYCARBONYL COMPOUNDS

	Carbonyl Compound	Reagent	Product	Yield, %	Reference
		α-Diketones			
$C_4H_6O_2$	Biacetyl	Perphthalic acid	Acetic acid	24	67, 61
$C_5H_8O_3$	Ethyl pyruvate	Perphthalic acid	Monoethyl ester of acetic-carbonic anhydride	—	8
$C_6Br_4O_2$	Tetrabromo-*o*-benzoquinone	$C_6H_5CO_3H$	2,3,5-Tribromo-4-hydroxymuconolactone	30	17, 154
$C_6Cl_4O_2$	Tetrachloro-*o*-benzoquinone	Perphthalic acid	2,3,5-Trichloro-4-hydroxymuconolactone, tetrachloromuconic acid	4 31	155
$C_6H_4O_2$	*o*-Benzoquinone	CH_3CO_3H	*cis,cis*-Muconic acid	—	61
$C_6H_{10}O_2$	Hexane-3,4-dione	Perphthalic acid	Propionic acid	—	67
$C_7H_6O_2$	*p*-Methyl-*o*-benzoquinone	Perphthalic acid	β-Methylmuconic anhydride	22	65
$C_8H_6O_3$	Ethyl phenylglyoxalate	Perphthalic acid	Monoethyl ester of benzoic-carbonic anhydride	—	8
$C_9H_7NO_5$	*o*-Nitrophenylpyruvic acid	H_2O_2, NaOH	*o*-Nitrophenylacetic acid	92	62
$C_9H_{12}O_3$	1,2,4-Triketo-3,3,5,5-tetramethylcyclopentane	H_2O_2	Tetramethylacetonedicarboxylic acid	Quantitative	79
$C_{10}H_6O_2$	β-Naphthoquinone	CH_3CO_3H	*o*-Carboxy*allo*cinnamic acid	76	61
		$C_6H_5CO_3H$	*o*-Carboxy*allo*cinnamic anhydride	22	17
		CH_3CO_3H	Phthalic acid	—	156
$C_{11}H_8O_3$	6-Methoxy-1,2-naphthoquinone	Perphthalic acid	2-Carboxy-5-methoxycinnamic acid	23	59
		CH_3CO_3H	2-Carboxy-5-methoxycinnamic acid	31	59
$C_{12}H_5BrO_8$	β-Bromolaccain	H_2O_2, CH_3CO_2H	4-Ketocarboxy-2,3,5-tricarboxyphenol (?)	—	157
$C_{12}H_6O_2$	Acenaphthenequinone	CH_3CO_3H	Naphthalic acid	—	156
$C_{14}H_6N_4O_{10}$	2,2′,4,4′-Tetranitrobenzil	H_2O_2, NaOH	2,4-Dinitrophenol	53	72
		H_2O_2, CH_3CO_2H	2,4-Dinitrobenzoic acid	Quantitative	72
$C_{14}H_8O_2$	9,10-Phenanthraquinone	H_2O_2, NaOH	Diphenic acid	94	136, 156
$C_{14}H_{10}O_2$	Benzil	$C_2H_5O_2H$, NaOH	Benzoic acid, ethyl benzoate	70	158
		CH_3CO_3H	Benzoic acid	95	61, 70
		H_2O_2, CH_3CO_2H, $HClO_4$	Benzoic acid	83	6
$C_{15}H_{12}O_2$	1,3-Diphenylpropane-1,2-dione	$C_2H_5O_2H$, NaOH	Benzoic acid, phenylacetic acid	61	158
$C_{15}H_{12}O_3$	*p*-Methoxybenzil	$C_2H_5O_2H$, NaOH	Anisic acid, benzoic acid	79	158
$C_{16}H_{14}O_4$	Anisil	$C_2H_5O_2H$, NaOH	Anisic acid, ethyl anisoate	70	158
		H_2O_2, CH_3CO_2H	Anisic acid	66	6
$C_{18}H_{14}O_2$	Dicinnamylidenebiacetyl	Perphthalic acid	2-Styrylacrylic anhydride	26	66

Note: References 138-164 are listed on p. 106.

TABLE V—*Continued*

BAEYER-VILLIGER OXIDATION OF POLYCARBONYL COMPOUNDS

	Carbonyl Compound	Reagent	Product	Yield, %	Reference
		α-Diketones—Continued			
$C_{18}H_{18}O_2$	1-Mesityl-3-phenylpropane-1,2-dione	$C_2H_5O_2H$, NaOH	Phenylacetic acid, β-isodurylic acid	70	158
$C_{18}H_{32}O_4$	9,10-Diketostearic acid	CH_3CO_2H	Pelargonic acid, azelaic acid	90–95	61
$C_{21}H_{32}O_5$	3β,14-Dihydroxy-14-iso-20-keto-17-iso-pregnan-21-carboxylic acid	H_2O_2, CH_3CO_2H	3β,14-Dihydroxy-14-iso-17-isoetiocholanic acid	27	68
		H_2O_2, $KHCO_3$	3β,14-Dihydroxy-14-iso-17-isoetiocholanic acid	90	68
$C_{23}H_{32}O_5$	3β-Acetoxy-14-hydroxy-14-iso-20-keto-pregnan-21-carboxylic acid lactone	H_2O_2, CH_3CO_2H	3β-Acetoxy-14-hydroxy-14-isoetiocholanic acid	—	68
		β-Diketones			
$C_5H_8O_2$	Acetylacetone	CH_3CO_3H	Ethanol	—	77
$C_6H_{10}O_3$	Ethyl acetoacetate	CH_3CO_3H	Ethyl hydrogen oxalate, ethanol	—	77
$C_7H_{12}O_2$	3,3-Dimethylpentane-2,4-dione	CH_3CO_3H	No reaction	—	77
$C_7H_{12}O_3$	Ethyl α-methylacetoacetate	CH_3CO_3H	Ethyl hydrogen oxalate	—	77
$C_8H_{14}O_3$	Ethyl α,α-dimethylacetoacetate	CH_3CO_3H	No reaction	—	77
$C_9H_{14}O_5$	Ethyl acetonedicarboxylate	CH_3CO_3H	Oxalic acid	—	77
$C_{11}H_8O_3$	2-Acetylindan-1,3-dione	H_2O_2, $(C_2H_5)_2O$	2-Acetoxyindan-1,3-dione	64	78
$C_{11}H_{12}O_3$	Ethyl benzoylacetate	CH_3CO_3H	Benzoic acid, ethyl oxalate	—	77
$C_{13}H_{16}O_3$	Ethyl α-benzylacetoacetate	CH_3CO_3H	Ethyl hydrogen oxalate, methylbenzylcarbinol	—	77
$C_{14}H_{20}O_2$		H_2O_2, CH_3CO_2H		87	118
$C_{15}H_{22}O_4$	1-Isovaleryl-2,4,6-triketo-3,3,5,5-tetramethylcyclohexane (leptospermone)	H_2O_2, pyridine	2,4,6-Triketo-3,3,5,5-tetramethylcyclohexyl isovalerate	12	79
$C_{16}H_{10}O_3$	2-Benzoylindan-1,3-dione	H_2O_2, $(C_6H_5)_2O$	2-Benzoyloxyindan-1,3-dione	66	78
$C_{17}H_{14}O_3$	Acetyldibenzoylmethane	H_2O_2, $(C_2H_5)_2O$	No reaction	—	78
$C_{22}H_{16}O_3$	Tribenzoylmethane	H_2O_2, NaOH	Benzoic acid	92	78

Note: References 138-164 are listed on p. 106.

TABLE VI

BAEYER-VILLIGER OXIDATION OF ALDEHYDES

	Carbonyl Compound	Reagent	Product	Yield, %	Reference
CH_2O	Formaldehyde	CH_3CO_3H	Formic acid	Quantitative	80
		H_2O_2, NaOH	Formic acid, hydrogen	—	89, 87
C_2H_4O	Acetaldehyde	$C_6H_5CO_3H$	Acetic acid	—	81
		H_2O_2, H_2SO_4	Acetic acid, formic acid, methane, hydrogen, carbon dioxide	—	88
$C_2H_4O_2$	Glycolic aldehyde	H_2O_2	Hydrogen, carbon dioxide, formic acid, unidentified acids	—	86
C_3H_6O	Propionaldehyde	H_2O_2, H_2SO_4	Propionic acid, acetic acid, formic acid, hydrogen. carbon dioxide, ethane	—	88
$C_5H_{10}O$	Pivalic aldehyde	H_2O_2	Isobutane, hydrogen, carbon monoxide, unidentified acids	—	86
$C_7H_4Br_2O_2$	3,5-Dibromo-2-hydroxybenzaldehyde	H_2O_2, NaOH	3,5-Dibromocatechol	—	52
	3,5-Dibromo-4-hydroxybenzaldehyde	H_2O_2, NaOH	3,5-Dibromohydroquinone	—	52
	4,6-Dibromo-2-hydroxybenzaldehyde	H_2O_2, NaOH	4,6-Dibromocatechol	—	52
$C_7H_4Cl_2O_2$	3,5-Dichloro-4-hydroxybenzaldehyde	H_2O_2, NaOH	3,5-Dichlorohydroquinone	—	52
	3,5-Dichloro-2-hydroxybenzaldehyde	H_2O_2, NaOH	3,5-Dichlorocatechol	—	159, 52
$C_7H_4I_2O_2$	3,5-Diiodo-4-hydroxybenzaldehyde	H_2O_2, NaOH	No reaction	—	52
$C_7H_5BrO_2$	5-Bromo-2-hydroxybenzaldehyde	H_2O_2, NaOH	5-Bromocatechol	—	52
	3-Bromo-4-hydroxybenzaldehyde	H_2O_2, NaOH	Bromohydroquinone	60–70	52
$C_7H_5ClO_2$	5-Chloro-2-hydroxybenzaldehyde	H_2O_2, NaOH	5-Chlorocatechol	—	52
$C_7H_5NO_3$	*o*-Nitrobenzaldehyde	CH_3CO_3H	*o*-Nitrobenzoic acid	99	91
	m-Nitrobenzaldehyde	CH_3CO_3H	*m*-Nitrobenzoic acid	90	91
$C_7H_5NO_4$	3-Nitro-2-hydroxybenzaldehyde	H_2O_2, NaOH	3-Nitrocatechol	—	52
	5-Nitro-2-hydroxybenzaldehyde	H_2O_2, NaOH	5-Nitrocatechol	70	52
	2-Nitro-3-hydroxybenzaldehyde	H_2O_2, NaOH	No reaction	—	52
	2-Nitro-4-hydroxybenzaldehyde	H_2O_2, NaOH	Nitrobenzoquinone	—	52
	3-Nitro-4-hydroxybenzaldehyde	H_2O_2, NaOH	No reaction	—	52
C_7H_6O	Benzaldehyde	H_2SO_5	Benzaldehyde peroxide	40	160, 140
		H_2O_2, $(C_2H_5)O$	Benzoic acid, phenol	—	92, 161
		CH_3CO_3H	Benzoic acid	Quantitative	80, 86
$C_7H_6O_2$	Salicylaldehyde	H_2O_2, CH_3COCH_3	Salicylic acid, catechol	70, trace	95

Note: References 138-164 are listed on p. 106.

TABLE VI—*Continued*

BAEYER-VILLIGER OXIDATION OF ALDEHYDES

	Carbonyl Compound	Reagent	Product	Yield, %	Reference
$C_7H_6O_2$	Salicylaldehyde (Contd.)	H_2O_2, pyridine	Salicylic acid, catechol	75, 20	95
		H_2O_2, NaOH	Catechol	Quantitative	52, 134
		CH_3CO_3H	Catechol	89	162, 91, 95
	m-Hydroxybenzaldehyde	H_2O_2, NaOH	No reaction	—	52
		CH_3CO_3H	*m*-Hydroxybenzoic acid	74	91
	p-Hydroxybenzaldehyde	H_2O_2, NaOH	Hydroquinone	Quantitative	52
		CH_3CO_3H	Hydroquinone	93	80, 91
$C_7H_6O_3$	2,4-Dihydroxybenzaldehyde	H_2O_2, NaOH	Hydroxyhydroquinone	—	52
	3,4-Dihydroxybenzaldehyde	H_2O_2, NaOH	Hydroxyhydroquinone	—	52
C_7H_7NO	*o*-Aminobenzaldehyde	H_2SO_5	*o*-Aminophenyl formate, *o*-aminophenol, anthranil	31	93
$C_7H_{14}O$	*n*-Heptanal	CH_3CO_3H	*n*-Heptanoic acid	88	80
		H_2O_2, $(C_2H_5)_2O$	α-Hydroxyheptylhydroperoxide	—	11
$C_8H_6O_3$	Piperonal	CH_3CO_3H	3,4-Methylenedioxyphenol	60	129
	2-Hydroxy-4-methylbenzaldehyde	CH_3CO_3H	4-Methylcatechol	70	91
	2-Hydroxy-5-methylbenzaldehyde	CH_3CO_3H	5-Methylcatechol	54	91
$C_8H_7BrO_3$	3-Bromo-4-hydroxy-5-methoxybenzaldehyde	H_2O_2, NaOH	3-Bromo-5-methoxyhydroquinone	45	52
$C_8H_7NO_5$	2-Nitro-4-hydroxy-3-methoxybenzaldehyde	H_2O_2, NaOH	3-Methoxy-2-nitrohydroquinone	—	52
	3-Nitro-4-hydroxy-5-methoxybenzaldehyde	H_2O_2, NaOH	No reaction	—	52
C_8H_8O	Phenylacetaldehyde	H_2O_2	Benzyl alcohol, formic acid	—	163
		H_2O_2, heat	Phenylacetic acid, benzaldehyde, formic acid, benzoic acid	—	163
$C_8H_8O_2$	*o*-Methoxybenzaldehyde	H_2O_2, $(C_2H_5)_2O$	Guaiacol, *o*-methoxybenzoic acid	—	92
		CH_3CO_3H	Guaiacol formate	99	91
	p-Methoxybenzaldehyde	H_2O_2, $(C_2H_5)_2O$	Hydroquinone monomethyl ether, *p*-methoxybenzoic acid	—	92
		CH_3CO_3H	*p*-Methoxybenzoic acid	Quantitative	80
$C_8H_8O_3$	2-Hydroxy-3-methoxybenzaldehyde	H_2O_2, NaOH	3-Methoxycatechol	68–80	135
	2-Hydroxy-5-methoxybenzaldehyde	H_2O_2, NaOH	4-Methoxycatechol	—	159
	3-Hydroxy-4-methoxybenzaldehyde	H_2O_2, NaOH	4-Methoxyresorcinol (?)	—	52
	Vanillin	H_2O_2, NaOH	Methoxyhydroquinone	Quantitative	52

TABLE VI—*Continued*

BAEYER-VILLIGER OXIDATION OF ALDEHYDES

	Carbonyl Compound	Reagent	Product	Yield, %	Reference
$C_9H_{10}O_3$	2,4-Dimethoxybenzaldehyde	H_2O_2, $(C_2H_5)_2O$	2,4-Dimethoxyphenol	27	92
	3,4-Dimethoxybenzaldehyde	H_2O_2, $(C_2H_5)_2O$	3,4-Dimethoxyphenol, 3,4-dimethoxybenzoic acid	—	92
		CH_3CO_3H	3,4-Dimethoxyphenol	66	90, 91
$C_9H_{18}O$	Pelargonic aldehyde	H_2O_2, $(C_2H_5)_2O$	α-Hydroxynonylhydroperoxide	—	11
$C_{10}H_{12}O_3$	3-Ethoxy-4-methoxybenzaldehyde	CH_3CO_3H	3-Ethoxy-4-methoxyphenol	—	90
$C_{10}H_{12}O_4$	2,4,5-Trimethoxybenzaldehyde	H_2O_2, $(C_2H_5)_2O$	2,4,5-Trimethoxyphenol	18	92
$C_{10}H_{20}O$	Capric aldehyde	H_2O_2, $(C_2H_5)_2O$	α-Hydroxydecylhydroperoxide	—	11
$C_{11}H_{14}O_3$	3,4-Dimethoxy-6-ethylbenzaldehyde	H_2O_2, $(C_2H_5)_2O$	3,4-Dimethoxy-6-ethylphenol, 3,4-dimethoxy-6-ethylbenzoic acid	—	92
$C_{11}H_{22}O$	Undecylic aldehyde	H_2O_2, $(C_2H_5)_2O$	α-Hydroxyundecylhydroperoxide	—	11
$C_{12}H_{16}O_3$	4-Butoxy-3-methoxybenzaldehyde	CH_3CO_3H	4-Butoxy-3-methoxyphenol	68	90
$C_{12}H_{24}O$	Lauric aldehyde	H_2O_2, $(C_2H_5)_2O$	α-Hydroxydodecylhydroperoxide	—	11
$C_{14}H_{11}NO_3S$	4-Nitro-2(*p*-tolylthio)benzaldehyde	H_2O_2, CH_3CO_2H	4-Nitro-2(*p*-toluenesulphonyl) benzoic acid	—	164
$C_{15}H_{10}O_2$	3-Hydroxy-4-formylphenanthrene	H_2O_2, NaOH	3,4-Dihydroxyphenanthrene	80	94

Note: References 138-164 are listed on p. 106.

REFERENCES TO TABLES

[138] Baeyer and Villiger, *Ber.*, **33**, 858 (1900).
[139] Baeyer and Villiger, *Ber.*, **33**, 124 (1900).
[140] Dilthey, Inckel, and Stephan, *J. prakt. Chem.*, [2] **154**, 219 (1940).
[141] Friess, *J. Am. Chem. Soc.*, **71**, 14 (1949).
[142] Marker, *J. Am. Chem. Soc.*, **62**, 2621 (1940).
[143] Buchi and Jeger, *Helv. Chim. Acta*, **32**, 540 (1949).
[144] Karrer and Haab, *Helv. Chim. Acta*, **32**, 973 (1949).
[145] Schroeter, German pat. 562,827 (*Chem. Zentr.*, I, **1933**, 127).
[146] Stoll and Scherrer, *Helv. Chim. Acta*, **13**, 142 (1930).
[147] Jacobsen, Picha, and Levy, *J. Biol. Chem.*, **171**, 81 (1947).
[148] Burckhardt and Reichstein, *Helv. Chim. Acta*, **25**, 821 (1942).
[149] Windaus, *Ber.*, **37**, 2027 (1904).
[150] Dakin, *Proc. Chem. Soc.*, **25**, 194 (1909).
[151] Hassall and Todd, *J. Chem. Soc.*, **1947**, 611.
[152] Inagaki, *J. Pharm. Soc. Japan*, **59**, 7 (1939) [*C. A.*, **33**, 3790 (1939)].
[153] Böeseken and Kremer, *Rec. trav. chim.*, **50**, 827 (1931).
[154] Karrer and Hohl, *Helv. Chim. Acta*, **32**, 1028 (1949).
[155] Karrer and Testa, *Helv. Chim. Acta*, **32**, 1019 (1949).
[156] Charrier and Beretta, *Gazz. chim. ital.*, **54**, 988 (1924).
[157] Dimroth and Goldschmidt, *Ann.*, **399**, 62 (1913).
[158] Barnes and Lewis, *J. Am. Chem. Soc.*, **58**, 947 (1936).
[159] Kvalnes, *J. Am. Chem. Soc.*, **56**, 2487 (1934).
[160] Baeyer and Villiger, *Ber.*, **33**, 2484 (1900).
[161] Sandonnini and Giacomello, *Atti reale accad. naz. Lincei*, [6] **19**, 43 (1934) (*Chem. Zentr.*, II, **1934**, 234).
[162] Wacek, Eppinger, and Bezard, *Ber.*, **73**, 521 (1940).
[163] Cattaneo, *Gazz. chim. ital.*, **64**, 509 (1934).
[164] Campbell, Dick, Ferguson, and Louden, *J. Chem. Soc.*, **1941**, 747.