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The Oxidation Potentials of Aldehydes and Ketones

BY HOMER ADKINS, RICHARD M. ELOFSON,[1a] A. G. ROSSOW[1b] AND COWIN C. ROBINSON

The relative strengths of ninety carbonyl compounds as oxidizing agents have been ascertained by determining the concentrations at equilibrium in systems of the type

$$R_2CO + R'_2CHOH \underset{}{\overset{Al(OC_4H_9\text{-}t)_3}{\rightleftharpoons}} R_2CHOH + R_2'CO.$$

The experimental observations on which the data in the table are based were made by F. W. Cox,[2] Robert H. Baker,[3,4] A. G. Rossow,[5] C. C. Robinson[6] and Richard M. Elofson.[7] The last named has calculated all the values given herewith, and has concluded[7] that except for benzaldehyde, the values previously published are high by 33 m.v.

The oxidation potentials were calculated on the basis of the oxidation potentials of certain quinones. Three quinones of known oxidation potentials[8] were included in the series, *i. e.*, 9,10-anthraquinone, 154 mv., 1-chloroanthraquinone, 174 mv. and isopropyl 9,10-anthraquinone-2-carboxylate, 222 mv. One ketone, 2,7-dichlorofluorenone, was equilibrated against each of the three quinones. The oxidation potential, E_0, of 2,7-dichlorofluorenone was calculated from the oxidation potential of a quinone E_0' using the expression $E_0 = E_0' + RT/NF \ln K$ where K is the equilibrium constant for the reaction given above. For 25° the expression becomes $E_0 = E_0' + 0.0296 \log K$.

The oxidation potential of the ketone was found to be 157, 156 or 160 mv. depending upon the quinone used in comparison. Fluorenone and benzophenone have also been equilibrated against each other and against 9,10-anthraquinone. These ketones were in turn equilibrated against cyclohexanone and the latter against 2,7-dichlorofluorenone. The values of E_0 for 2,7-dichlorofluorenone, calculated from these series of comparisons, were 154 and 159 mv. The average of the five values for 2,7-dichlorofluorenone is 157 mv. This figure has been used as the basis for calculating the oxidation potential of most of the carbonyl compounds listed in the Table I, since 2,7-dichlorofluorenone was equilibrated directly or indirectly against all the other ketones and aldehydes except chloral and the alpha-keto esters. These keto esters and chloral were equilibrated against isopropyl benzoylformate and the latter against isopropyl 9,10-anthraquinone-2-carboxylate.

Limitations and Reliability of Data

There are several factors which determine and limit the reliability of the procedures on which the data in Table I are based. The method for the determination of the concentration of the reactants at equilibrium depends upon at least one of the two carbonyl compounds in a reaction mixture showing a depolarization potential on a polarograph. Thus direct comparisons must include an aldehyde, or a quinone, or a ketone with unsaturation in the 2,3-position. The concentration of such carbonyl compounds can be determined so accurately with a polarograph[4] that if the analytical determination were the only source of error the calculated oxidation potential would in general be reliable within 1 or 2 mv.

The greater the difference in oxidation potential between the two carbonyl compounds in the reaction mixture, the less accurate is the calculated oxidation potential. Small errors in the analytical determination will cause relatively large errors in the calculated oxidation potential when the difference between E_0 and E_0' is more than about 50 mv. This follows from the fact that if two carbonyl compounds A and B differ in potential by 100 mv. then at equilibrium there will be only 2% of the ketone A having the higher potential and 98% of B. If the difference in potential is 80 mv. there will be 4.2% of A, for 60 mv. 8.8% A, for 50 mv. 12.5% A, for 30 mv. 23.5% A, for 20 mv. 31.5% A and for 10 mv. 40.5% A. In order to minimize errors arising from this source, fluorenone, 119 mv., 2,7-dichlorofluorenone, 157 mv., and isopropyl benzoylformate, 282 mv., were preferred for the measurement of carbonyl compounds having potentials in the three ranges. Cyclohexanone, 162 mv., has been used in equilibrations where the polarographic curve for 2,7-dichlorofluorenone was obscured by that of the other carbonyl compound in the reaction mixture. Benzaldehyde, 192 mv., and trimethylacetaldehyde, 211 mv., were also useful in determining the oxidation potential of other aldehydes in the range of 186 to 270 mv.

The most serious limitation upon the accurate determination of the oxidation potential of a carbonyl compound, by the procedures described herewith, is imposed by side reactions. These are particularly serious with carbonyl compounds which react slowly as oxidizing agents and yet are capable of undergoing the aldol or Tischenko types of condensation. The more rapid the oxidation by the reference compound the less

(1) Wisconsin Alumni Research Foundation Fellow (a) 1941-1944; (b) 1939-1942.

(2) Adkins and Cox, THIS JOURNAL, **60**, 1151 (1938); **61**, 3364 (1939).

(3) Baker and Adkins, *ibid.*, **62**, 3305 (1940).

(4) Baker and Schaefer, *ibid.*, **65**, 1675 (1943).

(5) A. G. Rossow, Ph.D. Thesis, Univ. of Wisconsin, 1942.

(6) C. C. Robinson, Ph.D. Thesis, Univ. of Wisconsin, 1943.

(7) R. M. Elofson, Ph.D. Thesis, Univ. of Wisconsin, 1944.

(8) Conant and Fieser, THIS JOURNAL, **46**, 1858 (1924).

TABLE I

SUMMARY OF OXIDATION POTENTIALS

No.	Compound	E_0, mv.	$-\Delta F^0$ 25°, cal.	Equilibrated against[a]	M. p., °C. or $n^{25}D$ Carbinol	Carbonyl	Dep. pot. (−)
1	Δ^4-Cholestenone	63	2.9	20E	140.5–141	80–81[c]	1.30[b]
2	α-Hydrindone	73	3.4	20Rb	66–68	41–42[d]	1.55
3	α-Tetralone	80	3.7	20Rs	1.5643	1.5662	1.67
4	Camphor	82	3.7	20B			
5	Δ^2-Cyclohexenone	85	3.9	20E	1.4828	1.4853	1.55[b]
6	*p*-Methoxyacetophenone	99	4.6	20Rb	1.5330	1.5310[e]	1.70
7	Di-isopropyl ketone	100	4.6	39C			
8	Di-*n*-butyl ketone	101	4.6	39C			
9	Di-*n*-propyl ketone	101	4.6	39C			
10	Di-isobutyl ketone	102	4.7	39C			
11	Di-ethyl ketone	110	5.1	39C			
12	Acenaphthenone	110	5.1	20Rb	144.5–145.5	120.5–121.5	
13	*n*-Propyl phenyl ketone	113	5.2	39C			
14	3,5-Dimethoxyphenyl *n*-butyl ketone	114	5.3	20Rb	1.5166	42–43[c]	1.56
15	1,4-Diphenylbutanone-1	115	5.3	20E	47.5–48	56–57[c]	
16	*p*-Methylacetophenone	115	5.3	20Rb	1.5186	1.5310[d]	1.66
17	Methyl cyclohexyl ketone	116	5.4	20B			
18	*n*-Butyl phenyl ketone	116	5.4	39C			
19	*n*-Amyl phenyl ketone	117	5.4	39C			
20	Fluorenone	117	5.4	58B	151–152	83–84	1.07[b]
	Fluorenone	119	5.5	55E			
21	Methyl phenyl ketone	118	5.4	20B			
22	Ethyl phenyl ketone	118	5.4	39C			
23	2-Fluorenyl methyl ketone	119	5.5	20Rb	137–138	128–129	1.51[b]
24	β-Acetonaphthone	120	5.5	20E	73–73.5	54.5–55[c]	1.65
25	*m*-Methoxyacetophenone	120	5.5	20Rb	1.5316	1.5383	1.65
26	1,3-Diphenylpropanone-1	121	5.6	20E	1.5685	72.5–73	1.61
27	Isopropyl 9-fluorenone-4-carboxylate	121	5.6	58Rb	93.5–95	89–90.5[c]	1.04[b]
28	Ethyl 9-fluorenone-4-carboxylate	121	5.6	58Rb		103	
29	Methyl *t*-butyl ketone	121	5.6	20B			
30	α-Furyl methyl ketone	122	5.6	20Rs	1.4763	1.5043	1.63
31	Ethyl methyl ketone	123	5.7	20B			
32	Methyl isopropyl ketone	123	5.7	20B			
33	Cyclopentanone	123	5.7	20B			
34	Xanthone	124	5.7	20B			
35	Isopropyl phenyl ketone	125	5.8	39C			
36	1-Naphthyl phenyl ketone	128	5.9	20Rb	86–87	76	1.46[b]
37	*m*-Tolyl phenyl ketone	128	5.9	20Rb	54–55	1.5965	1.57[b]
38	Dimethyl ketone	129	6.0	20B			
39	Diphenyl ketone	129	6.0	20B			
	Diphenyl ketone	126	5.8	55E			
40	*p*-Bromoacetophenone	129	6.0	20Rb	1.5689	49–51[c]	1.57
41	Phenyl benzyl ketone	136	6.3	20Rs	67–68	55.5–56	1.60[b]
42	Ethyl *p*-acetylbenzoate	136	6.3	20Rb	1.5062	54–56	1.35[b]
43	β-Hydrindone	139	6.4	20Rb	70–70.3	57–57.5	
44	Benzyl methyl ketone	140	6.5	20Rs	1.5187	1.5139	
45	Methyl 9-fluorenone-2-carboxylate	140	6.5	58Rb	118–119.5	184–185[c]	1.02[b]
46	2-Chlorofluorenone	141	6.5	58Rs	142–143	122–123	1.06[b]
47	*o*-Methoxyacetophenone	141	6.5	20Rb	1.5312	1.5378[c]	1.63
48	Ethyl benzoylacetate	147	6.8	20Rb	1.5107	102–3/1[f]	1.49[b]
49	Isopropyl *m*-benzoylbenzoate	149	6.9	58Rb	180–1/2[f]	1.5723[c]	1.38
50	*m*-Nitroacetophenone	152	7.0	20Rb	63	79.5–81[c]	0.80–1.67
51	Ethyl *p*-benzoylbenzoate	152	7.0	58E		54.5–55.5	1.27[b]
52	Isopropyl *p*-benzoylbenzoate	153	7.1	58E	51–52	55.5–56	1.26[b]
53	*t*-Butyl *p*-benzoylbenzoate	152	7.0	58E		49–50	1.27[b]
54	Δ^5-Cholestenone-3	153	7.1	20E	148		
55	9,10-Anthraquinone	154	7.1	Ref. 8			
56	β-Tetralone	155	7.2	20Rs	1.5632	1.5557	

TABLE I (*Continued*)

No.	Compound	E_0, mv.	$-\Delta F^0$ 25°, cal.	Equilibrated against	M. p., °C. or $n^{25}D$ Carbinol	Carbonyl	Dep. pot. (−)
57	2,7-Dichlorofluorenone	157	7.2	58Rs	161–162	192–193	0.84[b]–1.07
	2,7-Dichlorofluorenone	157	7.2	55E			
58	Cyclohexanone	162	7.5	20B			
59	Δ^3-Cyclohexenone	162	7.5	20E			
60	3-Methoxycyclohexanone	167	7.7	20Rs	1.4638	1.4558[d]	
61	4-Methoxycyclohexanone	167	7.7	20Rs	1.4661	1.4530	
62	β-Pyridyl phenyl ketone	167	7.7	58E	67.5–69	1.6060[c]	1.22[b]
63	*t*-Butyl phenyl ketone	169	7.8	20B			
64	*p*-Nitrobenzophenone	171	7.9	57E	73–74	136–137[c]	1.42
65	1-Chloroanthraquinone	175	8.1	57E		161–161.5	
	1-Chloroanthraquinone	174	8.0	Ref. 8			
66	Benzhydryl methyl ketone	182	8.4	20Rs	57.5–58.5	58–60	
67	Cinnamaldehyde	186	8.6	74E	1.5772	1.6120	1.08[b]
68	Methoxyacetone	189	8.8	57Rs	1.4010	1.3955	
69	α-Tetrahydrofuryl methyl ketone	195	9.0	57Rs	1.4461	1.4361	
70	Crotonaldehyde	194	9.0	74E	1.4262	1.4355[c]	1.37
71	Benzaldehyde	197	9.1	57E			1.34
72	Benzoin methyl ether	199	9.2	58Rs	54–61	47–48	1.52[b]
73	ω-Piperidinoacetophenone	203	9.4	58Rs	70.5–71.5	1.5396	1.25
74	Trimethylacetaldehyde	211	9.8	71E	54–55	1.3765	
75	Phenylglyoxal dimethyl acetal	212	9.8	58Rs	1.5097	1.5102[d]	
76	ω-Methoxyacetophenone	213	9.8	58Rs	1.5190	1.5319[c]	1.43
77	Furfuraldehyde	214	9.9	74E	1.4868	1.5248	
78	Dibenzyl ketone	216	10.0	57Rs	1.5691	35	
79	2-Methoxycyclohexanone	218	10.1	57Rs	1.4571	1.4519[d]	
80	Isobutyraldehyde	220	10.2	71E	1.3953	1.3713	
81	Isopropyl anthraquinone-2-carboxylate	219	10.2	57E	125 (*ca.*)	138–139[c]	0.55
	Isopropyl anthraquinone-2-carboxylate	222	10.2	Ref. 8			
82	Acetaldehyde	226	10.4	71E			1.87
83	*t*-Butylglyoxal	245	11.3	71E	1.4297	85	
84	Formaldehyde	270	12.5	71E			1.38
	Formaldehyde	257	11.9	Ref. 9			
85	Chloral	277	12.8	86E	55.5/13[f]	96.5/74.0[f,c]	
86	Isopropyl benzoyl formate	282	13.0	81E	1.4969	1.5035	1.05[b]
87	Ethyl pyruvate	297	13.8	86Rs	1.4110	1.4042	1.35
88	Isopropyl pyruvate	299	13.8	86E	1.4078	1.4036	1.45[b]
89	Ethyl oxomalonate	298	13.8	86E	1.4283	1.4190	
90	1,3-Dimethoxyacetone	350[g]	..	57Rs	1.4177	1.4161	
				86E			

[a] The carbonyl compound against which Cox (C), Baker (B), Rossow (Rs), Robinson (Rb), or Elofson (E) equilibrated a given compound is indicated in the fifth column of the table, by using the number of the carbonyl compound as given for the compound in the first column of the table. The values for the methoxyacetophenones, given by Baker and Schafer,[4b] are in agreement with the potentials listed in the table for these compounds, if they are based upon a potential for fluorenone of 117 mv., rather than upon the value 150 mv. reported earlier.[4a] [b] These depolarization potentials were observed in a 0.1 *N* ammonium chloride solution, while the others reported were in a 0.05 *N* tetramethylammonium hydroxide solution. [c], [d] and [e] These ketones were reduced to the corresponding alcohols with aluminum isopropoxide[c] or by catalytic hydrogenation over Raney nickel[d] or copper chromium oxide[e]. [f] Boiling points. [g] This is a minimum value.

chance there is for a significant amount of a side reaction. Fluorenone is outstanding in giving rapid reactions. 2,7-Dichlorofluorenone is less reactive while isopropyl benzoylformate reacts quite slowly. Cyclohexanone reacts rapidly but is itself subject to condensation.

The determination of the oxidation potentials of Δ^4-cholestenone-3, Δ^5-cholestenone-3, Δ^2-cyclohexenone and Δ^3-cyclohexenone involves certain peculiar difficulties and uncertainties. In the classical Oppenauer oxidation of cholesterol by acetone to Δ^4-cholestenone-3 there is an intramolecular as well as an intermolecular oxidation–reduction. The latter ketone may be isolated in a yield of about 80% from such a reaction mixture. The reactions may be represented by the scheme

$$\begin{array}{ccc} \Delta^5\text{-cholestenol-3} + K & \rightleftharpoons & \Delta^5\text{-cholestenone-3} + A \\ \uparrow\downarrow & & \uparrow\downarrow \\ \Delta^4\text{-cholestenol-3} + K & \rightleftharpoons & \Delta^4\text{-cholestenone-3} + A \end{array}$$

where K represents a ketone and A the alcohol corresponding to it.

Cholesterol (Δ^5-cholestenol-3) is oxidized by

fluorenone, under our standard conditions of reaction, until at equilibrium the concentration of fluorenone is 80%. The conversion at equilibrium corresponds to a value of 153 mv. for Δ^5-cholestenone-3. The concentration of fluorenone at equilibrium with Δ^4-cholestenone-3, *i. e.*, 11%, corresponds with an oxidation potential of 63 mv. for the Δ^4-cholestenone-3, but the equilibrium then shifts in the direction of increasing fluorenone concentration. These facts are compatible with the hypothesis that in the oxidation of cholesterol to Δ^4-cholestenone-3 by ketones such as acetone and fluorenone, the Δ^5-cholestenone-3 is first formed and then undergoes intramolecular oxidation–reduction and the formation of the isomeric Δ^4-cholestenone-3.

Δ^2-Cyclohexenone and fluorenol or Δ^2-cyclohexenol and fluorenone give a similar series of changes which presumably involved the formation of Δ^3-cyclohexenol and Δ^3-cyclohexenone, *i. e.*

$$\Delta^3\text{-cyclohexenol} + K \rightleftarrows \Delta^3\text{-cyclohexenone} + A$$

$$\Delta^2\text{-cyclohexenol} + K \rightleftarrows \Delta^2\text{-cyclohexenone} + A$$

These intramolecular changes will be discussed in a subsequent paper; however, it should be pointed out that the conclusions as to the potential of the four ketones just discussed did not involve the isolation of Δ^5-cholestenone-3, Δ^3-cyclohexenone nor Δ^3-cyclohexenol.

Many of the ketones react so slowly that it was necessary to approach equilibrium concentrations by a series of approximations. After the probable ratio of the two ketones at equilibrium had been estimated, several reaction mixtures of the two ketones, R_2CO and $R_2'CO$, and the corresponding alcohols were made up. The ratios of reactants were varied so that in some mixtures there was slightly more and in some slightly less of R_2CO than at equilibrium. Determination of the direction and extent of shift could then be made after relatively short periods of reaction that minimized the effect of any side reactions.

Due to uncertainty as to the precise concentrations at equilibrium, the oxidation potentials given for formaldehyde, Δ^3-cyclohexenone, cinnamaldehyde, the α-methoxy ketones, ω-piperidinoacetophenone, *t*-butylglyoxal, chloral, isopropyl and ethyl pyruvates, Δ^4- and Δ^5-cholestenone-3 and ethyl oxomalonate may be in error by as much as $\pm$ 10 mv. Only a minimum value can be given for 1,3-dimethoxyacetone. The values for other equilibria, except as noted below, may be considered as accurate to within $\pm$5 mv. Relative to each other, the potentials of most of the ketones having values from about 110 to 170 mv. are probably reliable to within $\pm$3 mv. All equilibria except as noted were approached from both directions.

The equilibrium between formaldehyde and benzaldehyde could only be approached from one direction, *i. e.*, through the reaction of methanol and benzaldehyde. However, the value determined, 270 mv., is in fair agreement with the value of 257 mv. calculated from thermal data.[9] The earlier data in Parks and Huffman[10] indicate an oxidation potential of 277 mv.

The oxidation potentials of acetaldehyde, acetone and pyruvic acid have been reported, or may be calculated from data in the literature, and so compared with the potentials determined in this Laboratory. The oxidation potential of acetone, calculated from the data of Parks and Huffman,[10] is 126 mv. Later measurements by Dolliver, Gresham, Kistiakowsky and Vaughan[11] indicate that the value should be lower, *i. e.*, 121 mv. From Conant's[12] work it can be concluded that the oxidation potential of 9,10-anthraquinone in the gas phase is not more than 10–20 mv. lower than in solution. Thus the value of 129 mv. reported here for acetone is in agreement with those calculated from thermal data.

The free energy of reduction of acetaldehyde in the gas phase reported by Parks and Huffman is only 7,320 calories. However, they state that this value leads to an inconsistency of 2,230 calories in the free energy of formation, calculated for gaseous acetaldehyde. If such a correction is made, we find that $\Delta F^\circ_{298} = -9550$ cal., and $E_0 = 207$ mv. for acetaldehyde. The data given by Kistiakowsky and associates indicate that $\Delta F^\circ_{298} \approx -9400$ cal., assuming an entropy of 60 e. u. for acetaldehyde. However, until the entropy of gaseous acetaldehyde is measured, an accurate estimate of the free energy of reduction of gaseous acetaldehyde is not available. The oxidation potential measured by equilibration is 226 mv., which is in satisfactory agreement with the approximate values calculated above, since the values in solution are presumably 10 or 20 mv. higher than in the gas phase reaction.[12]

Three groups of investigators[13,14,15] have reported the oxidation potential of pyruvic acid in solution to be 288 mv. while two other groups[16,17] give higher values of 316 and 325 mv. The value reported here is 297–299 mv. for two esters of pyruvic acid. Conant and Fieser[8] have shown that in the quinone series the potential of an acid is about 10 mv. lower than for the ester. Thus the value for pyruvic acid would be 287–289 mv. which is in perfect agreement with that reported by three groups of investigators.

(9) Thompson, *Trans. Faraday Soc.*, **37**, 249 (1941).

(10) Parks and Huffman, "Free Energies of Some Organic Compounds," The Chemical Catalog Co., New York, N. Y., 1932.

(11) Dolliver, Gresham, Kistiakowsky and Vaughan, THIS JOURNAL, **59**, 831 (1937).

(12) Conant, *ibid.*, **54**, 2881 (1932).

(13) Barron and Hastings, *J. Biol. Chem.*, **107**, 567 (1933).

(14) Banga, Laki and Szent-Györgi, *Z. physiol. Chem.*, **217**, 43 (1933).

(15) Wurmser and Meyer, *J. chim. phys.*, **30**, 429 (1933).

(16) Baumberger, Jurgens and Bardwell, *J. Gen. Physiol.*, **16**, 961 (1933).

(17) Ganguli, *J. Indian Chem. Soc.*, **14**, 656 (1937).

Attention should be called to two assumptions made in the calculations of the potentials given in the table. The oxidation potentials for the quinones used for reference were determined in an alcohol–water solution,[8] while the equilibria were measured in toluene solution in the presence of aluminum alkoxides. The equilibria were in most instances established at 60 to 70°. In the calculations it is assumed that the value of K is the same at these temperatures as at 25°. The heat of the oxidation–reduction reaction is small and measurements with the aldehydes showed that the concentrations at equilibrium at 25° were the same as at 60°. Neither of these assumptions would affect the relative values of the oxidation potentials given herewith, but might distort the absolute values. However, the agreement between the values of E_0 calculated from physical chemical data and those from our experimental results supports the thesis that the absolute as well as the relative values of E_0 as given are reliable for the carbonyl compounds reported.

Relations of Structure and Oxidation Potential

There is a wide difference in oxidation potentials of carbonyl compounds depending upon the associated structures. The oxidation potential, or the free energy of reduction, is approximately five times as large for the highest as for the lowest member of the group of compounds reported here. The magnitude of this variation from a practical standpoint may be illustrated by a comparison of Δ^4-cholestenone-3 63 mv., cyclohexanone 162 mv., formaldehyde 270 mv., and dimethoxyacetone 350 mv. *Each* of these compounds would oxidize the alcohol corresponding to the *preceding* member of the series in a conversion of about 98%.

However, the potentials of the majority of ketones apparently lie within the range of 110 to 160 mv. The potentials of about half the ketones determined lie within this range despite the fact that compounds of lower and particularly of higher potentials were being sought. The potentials of the aldehydes lie somewhat higher, *i. e.*, in the range 220 to 270 mv.

Replacement of Hydrogen by Alkyl or Aryl Groups.—The replacement of hydrogen on a carbonyl by an alkyl or aryl group lowers the oxidation potential of a carbonyl compound. This is illustrated by the series H_2CO 260 mv., CH_3CHO 226 mv. and $(CH_3)_2CO$ 129 mv. Replacement of a hydrogen on a carbon adjacent to the carbonyl has a similar but much less marked effect, *e. g.*, CH_3CHO 226 mv., $(CH_3)_2CHCHO$ 220 mv. and $(CH_3)_3CCHO$ 211 mv. There is a similar effect in a series of open-chain ketones, which may be considered as related to acetone.

There are many alkyl and aryl groups which compared with methyl manifest little difference in effect upon the potential of the carbonyl group. There are perhaps twenty-five ketones listed in the table which show relatively little difference in potential as compared with acetone. Yet among this group of ketones are such diverse structures as in acetophenone, cyclopentanone, xanthone, benzophenone, fluorenone and the acetylnaphthalenes. No doubt there are among this group of ketones counterbalancing effects where one group tends to raise while another tends to lower the potential of the carbonyl group.

Four ketones have surprisingly high potentials, *i. e.*, cyclohexanone 162 mv., *t*-butyl phenyl ketone 169 mv., benzhydryl methyl ketone 182 mv. and dibenzyl ketone 216 mv. The high oxidation potentials of at least two of the ketones just mentioned, as well as many other observations reported in this paper, have been rationalized in the electronic terms of the English school.[7]

Effect of Unsaturation.—The presence of carbon-to-carbon double bonds in the 2,3-position with respect to a carbonyl brings about a distinct lowering of the oxidation potential. A comparison of benzaldehyde 197 mv., crotonaldehyde 194 mv. and cinnamaldehyde 186 mv., with a saturated aldehyde, acetaldehyde 226 mv. or isobutyraldehyde 220 mv., shows a lowering of 20 to 40 mv. An even more marked lowering of potential as compared with acetone 129 mv., is shown by Δ^4-cholestenone 63 mv., α-hydrindone 73 mv., α-tetralone 80 mv. and Δ^2-cyclohexenone 85 mv. α-Furyl methyl ketone 122 mv., is 73 mv. lower than the corresponding saturated ketone.

Carbon-to-carbon unsaturation in the 3,4-position with respect to the carbonyl has little or no effect upon the potential. Apparently Δ^3-cyclohexenone and cyclohexanone have the same potential of 162 mv. β-Tetralone 155 mv., and β-hydrindone 139 mv., have potentials similar to the corresponding alkyl aryl ketones. Δ^5-Cholestenone has a potential 90 mv. higher than the Δ^4-isomer. The unsaturation of the phenyl group does not in many instances have any marked effect on the potential when it replaces a methyl group in a methyl ketone. Acetone, benzophenone and acetophenone all have potentials in the range of 118–129 mv. However, in α-tetralone and benzaldehyde the potentials are considerably lower than for similar saturated cyclic compounds.

Effect of Ring Structures.—The very low oxidation potentials of certain cyclic ketones such as camphor, Δ^4-cholestenone, α-hydrindone and α-tetralone would not be anticipated from a knowledge of open-chain and aryl ketones. The high oxidation potential of cyclohexanone must result from the ring structure. However, the potential of cyclopentanone is in accord with that of open-chain compounds.

Effect of Alkoxy, Carbonyl and Carbalkoxy Groups.—The replacement of hydrogen by oxygen in the alpha position in a ketone results in a marked increase in the oxidation potential of the

carbonyl. This is shown by a comparison of acetone 129 mv., methoxyacetone 189 mv. and dimethoxyacetone of more than 350 mv. The ω-mono- and dimethoxyacetophenones, $C_6H_5COCH_2OCH_3$ and $C_6H_5COCH(OCH_3)_2$ show potentials of 212–213 mv., about 95 mv. higher than the corresponding non-oxygenated ketone acetophenone. α-Tetrahydrofuryl methyl ketone 195 mv., is 60–70 mv. higher than ketones without oxygen α to the carbonyl.

The α-methoxy ketone $C_6H_5CH(OCH_3)COC_6H_5$ 199 mv. is 59 mv. higher than the corresponding benzyl phenyl ketone 140 mv. 2-Methoxycyclohexanone 218 mv. is 56 mv. higher than cyclohexanone.

If the series of compounds $C_6H_5COCH_3$ 118 mv., $C_6H_5COCH_2OCH_3$ 213 mv., $C_6H_5COCH(OCH_3)_2$ 212 mv. and $C_6H_5COCO_2C_3H_7$ 282 mv. be considered to involve a progressive oxidation of the carbon atom α to the carbonyl to the alcohol, aldehyde and carboxylic acid stages, then it may be considered that the first step in oxidation of methylene increases the potential of the ketone by 95 mv. The second step in oxidation to the aldehyde or ketone is without effect, while the third step of oxidation to the acid raises the potential of the ketone group almost as much as the first. A similar effect is evident in the series CH_3COCH_3 129 mv., $CH_3COCH_2OCH_3$ 189 mv., and $CH_3COCO_2C_3H_7$ 299 mv. although in this series the third step in oxidation is more effective than the first. In both series the difference in potential between the simple ketone and the α-keto ester is quite large, *i. e.*, 164–170 mv.

Alkoxy and carbalkoxy groups more distant from a carbonyl than in the α-substituted compounds just considered, are considerably less effective in raising the oxidation potential. *m*-Methoxyacetophenone had a potential almost identical with acetophenone, while *o*-methoxyacetophenone was 22 mv. higher and *p*-methoxyacetophenone 19 mv. lower than acetophenone. The 3- and 4-methoxycyclohexanones had potentials little different from cyclohexanone. The carbalkoxy substituted ketones such as items 42, 45, 48, 49, 51, 52 and 53 in the table show potentials 18 to 29 mv. higher than the corresponding unsubstituted ketones.

The potential of an α-keto aldehyde was found to be considerably higher than for an aldehyde of somewhat similar structure but without an α-carbonyl group, *i. e.*, *t*-butylglyoxal was 34 mv. higher than trimethylacetaldehyde. The effect of free hydroxyl or carbonyl groups on the oxidation potential of a carbonyl group cannot in general be determined because of the multiplicity of equilibria which would be involved. However, the potential of *t*-butylglyoxal could be evaluated since the *t*-butyl group served to inactivate the adjacent carbonyl toward reduction.

Effect of Amino and Nitro Groups and of Halogens.—The substitution of a nitrogen for hydrogen α to carbonyl, like the substitution of an oxygen, gave a marked increase in potential. ω-Piperidinoacetophenone with a potential of 203 mv. is 85 mv. higher than acetophenone. Nitrogen in the β-position with respect to the carbonyl also enhances the potential. β-Pyridyl phenyl ketone with a potential of 167 mv. is about 40 mv. above benzophenone. The introduction of a nitro group in the meta position of acetophenone and in the para position in benzophenone also raised the potentials by 34 and 42 mv., respectively.

The substitution of a chlorine for a hydrogen in a ketone has given in certain instances a marked increase in oxidation potential. The 2-chlorofluorenone and 2,7-dichlorofluorenone were prepared and tested because Conant and Fieser[8] had noted that certain chloroquinones had higher oxidation potentials than the parent compounds. The discovery[5] of the relatively high potential of the dichlorofluorenone, 157 mv., as compared to 117 mv. for fluorenone, was one of the important steps in making possible the determination of the potential of ketones high in the series. The effectiveness of chlorine substitution in raising the oxidation potential is very evident in a comparison of chloral 277 mv., with acetaldehyde 226 mv.

Rate of Reaction.—There is a very considerable difference in the rate with which equilibrium is established with different carbonyl compounds. Quantitative data on the rates of reaction are not available and in many cases significant numerical values are not obtainable because of side reactions. However, it may be significant to note some of the facts encountered.

Aldehydes such as acetaldehyde, trimethylacetaldehyde, isobutyraldehyde, furfural and benzaldehyde reach equilibrium within an hour or less at 60°. Certain ketones such as cyclohexanone and acetone react with fluorenol almost as rapidly as the aldehydes mentioned. The cyclic ketones β-hydrindone, the two tetralones and the 3- and 4-methoxy cyclohexanones react rather rapidly, only a few hours being required for the attainment of equilibrium. Many ketones such as acetophenone, furyl methyl ketone and benzophenone require twelve to forty-eight hours to reach equilibrium even with fluorenol. The α-oxygenated ketones and aldehydes, chloral, β-pyridyl phenyl ketone, ω-piperidinoacetophenone, tetrahydrofuryl methyl ketone and the carbethoxy ketones react very slowly indeed so that one hundred to one thousand hours would be required for the attainment of equilibrium.

Depolarization Potentials of Carbonyl Compounds.—The oxidation potential of a quinone may be calculated from its depolarization potential at a dropping mercury electrode.[18,19,20]

(18) Miller and Baumberger, *Trans. Electrochem. Soc.*, **71**, 169 (1937).

(19) Smith, Kolthoff, Wawzonek and Ruoff, THIS JOURNAL, **63**, 1018 (1941).

(20) Arnold and Zaugg, *ibid.*, **63**, 1317 (1941).

TABLE II

ANALYSES OF COMPOUNDS

Name of compound	B. p. °C.	Mm.	Formula	Calcd., % Carbon	Calcd., % Hydrogen	Found, % Carbon	Found, % Hydrogen
Mandelaldehyde dimethyl acetal	126.5–127.5	10	$C_{10}H_{14}O_3$	65.9	7.7	65.7	7.8
3-Methoxycyclohexanone	76.5–77	9	$C_7H_{12}O_2$	65.6	9.4	65.3	9.3
Isopropyl 9-fluorenol-2-carboxylate	M. 118–119.5		$C_{17}H_{16}O_3$	76.1	6.0	75.9	5.9
Isopropyl *p*-benzoylbenzoate	190–192	2	$C_{17}H_{16}O_3$	76.1	6.0	76.1	5.9
t-Butyl *p*-benzoylbenzoate	190–192	2	$C_{18}H_{18}O_3$	76.6	6.4	76.7	6.2
4-Carbisopropoxy benzhydrol	209	4	$C_{17}H_{18}O_3$	75.5	6.7	75.2	6.8
Isopropyl benzoylformate	153.5–154.4	12	$C_{11}H_{12}O_3$	68.6	6.2	68.5	6.1
Isopropyl pyruvate	50.5–51	13	$C_6H_{10}O_3$	55.4	7.7	55.5	7.6
β-Pyridylphenylcarbinol	M. 67.5–69		$C_{12}H_{11}ON$	77.8	5.9	77.7	5.9
1-Chloro-10-oxanthrol	M. 135–137		$C_{14}H_9O_2Cl$	68.7	3.7	69.0	3.7
Isopropyl anthraquinone-2-carboxylate	M. 138–139		$C_{18}H_{14}O_4$	73.6	4.8	73.5	4.7
Methyl-*p*-carbethoxyphenylcarbinol	131	2	$C_{11}H_{14}O_3$	68.0	7.3	68.4	7.4
3-Carbisopropoxybenzohydrol	180–181	2	$C_{17}H_{18}O_3$	75.5	6.7	75.7	6.6

There has been no similar correlation observed between the oxidation potentials of aldehydes and ketones and their depolarization potentials.[4] The depolarization potential of many carbonyl compounds was determined at the dropping mercury electrode, incidental to the analytical procedure used in determining the concentration of carbonyl compounds at equilibrium. These values are given in the last column of Table I. The potential recorded is that applied between the falling droplets of mercury and the quiet pool of mercury at the bottom of the polarograph cell, when the diffusion current had attained one-half of its limiting value. A comparison of the depolarization potentials with the oxidation potentials of the carbonyl compounds in column three of Table I lends further support to the conclusion expressed above as to the lack of correlation between the two characteristics of a carbonyl compound. For example Δ^4-cholestenone-3 and ethyl pyruvate have similar depolarization potentials yet the oxidation potentials of the two carbonyl compounds lie almost at the extremes of the compounds listed in the table.

Procedures and Preparations of Reactants.—The procedures followed in equilibrating a quartet of carbonyl compounds and alcohols, and in determining the relative concentration of the compounds at equilibrium, were essentially those described earlier.[4] Since many of the sets of reactants reacted very slowly and gave side reactions it was usually necessary to make up many mixtures and carefully bracket the equilibrium mixture before drawing the final conclusion as to the true concentration at equilibrium. These data, even in abstract form, are so voluminous that they are not submitted for publication.

A few minor improvements in the procedures were introduced in order to avoid difficulties encountered from time to time. The addition of a drop of 0.25 *N* ammonium chloride solution facilitated the complete precipitation of aluminum hydroxide in the hydrolysis step. Care was taken to avoid the exposure of the alcohols or the reaction mixtures to strong sunlight at any stage of the procedure. An electrode of the type described by Kolthoff and Lingane[21] is more satisfactory than that used in earlier work. A stopcock without grease was inserted just above the flat-bottom capillary. The intervals between droplets of mercury were 2 ± 0.5 seconds.

Most of the carbonyl and carbinol compounds used in this investigation have been prepared earlier by others. Space was not available for publication of references to the earlier papers, however the references have been assembled.[5,6,7] Analytical data for compounds not previously described are given in Table II. The melting points or refractive indices of the alcohols and ketones used in the determinations, reported for the first time in this paper, are given in Table I. Several of the alcohols were prepared for the first time through the reduction of a ketone to the corresponding alcohol with aluminum isopropoxide or by catalytic hydrogenation over Raney nickel or copper-chromium oxide. These cases have been noted in Table I. Procedures for the preparation of a few compounds are given below.

2,7-Dichlorofluorenone and 2,7-Dichlorofluorenol.—Ten grams of pure, white, distilled fluorene, m. p. 110–112°, was chlorinated in 90 ml. of chloroform during one and one-half hours. The temperature of the mixture rose somewhat above room temperature due to heat of reaction but fell again to room temperature during the period of reaction. The solvent was blown off on a steam-bath and the residue recrystallized two or three times from petroleum ether (b. p. 90–100°). The yield was 5.4 g. (38%) of 2,7-dichlorofluorene, m. p. 123–124.5°. The compound (21 g.) was dissolved in 100 ml. of hot acetic acid and 65 g. of sodium dichromate in 100 ml. of acetic acid added slowly. The mixture was refluxed for thirty minutes and then poured into cold water. The product was separated by filtration and crystallized from a 1:4 mixture of benzene and petroleum ether (b. p. 90–100°). The yield of 2,7-dichlorofluorenone, m. p. 190–191° was 17.5 g. The ketone (9 g.) was reduced with zinc in an ammoniacal solution[22] to give 2,7-dichlorofluorenol (7.4 g.), m. p. 161–162°.

(21) Kolthoff and Lingane, *Chem. Revs.*, **24**, 1 (1939).

(22) Courtot, *Ann. chim.*, **14**, 5 (1930).

2-Chlorofluorenone and 2-Chlorofluorenol.—2-Aminofluorene[23] (15.8 g., m. p. 127–128°) was made into a paste on a steam-bath with 90 ml. of water. Concd. hydrochloric acid (16.5 ml.) in 185 ml. of water was added to the paste and the mixture allowed to cool to room temperature. The amine was diazotized with a solution of 6.1 g. of sodium nitrite in 45 ml. of water. The mixture, in which the diazonium salt had crystallized out, was poured with shaking into a solution of 25 g. of cuprous chloride in 125 ml. of concd. hydrochloric acid and refluxed for thirty minutes. After cooling, the solid material was filtered off, dried, pulverized and extracted with 500 ml. of ether. The ether solution was washed with a 5% solution of sodium hydroxide and dried over potassium carbonate. The ether was distilled off and the residue distilled 140–150° (2 mm.). The white solid product (10.5 g.) was recrystallized from 30 ml. of hot 95% alcohol giving 8.7 g. white 2-chlorofluorene m. p. 93–94°. The product was converted to 2-chlorofluorenone (8.0 g., m. p. 113–116° or 6.3 g., m. p. 122–123°) by oxidation as described for 2,7-dichlorofluorenone. The ketone (3.5 g.) was reduced to 2-chlorofluorenol (3.2 g., m. p. 142–143°) as by Courtot.

sym-Dimethoxyacetone.—Methyl methoxyacetate (101 g., b. p. 128–130° (740 mm.), $n^{25}D$ 1.3940) was prepared from methanol and chloroacetic acid (157 g.) as by Schreiner.[24] The ester was added to sodium methoxide (from 17 g. of sodium) and stirred for four hours on a steam-bath. The reaction mixture was then cooled, diluted with water and neutralized with acetic acid. The solution was extracted twice with ether and the latter washed with a sodium carbonate solution and dried over sodium sulfate. After removing the ether the desired dimethoxy keto ester was distilled at 114–115° (10 mm.). The yield was 31.8 g. having $n^{25}D$ of 1.4358. The ester was hydrolyzed in 200 ml. of a 5% sodium hydroxide solution for three hours on the steam-bath. The reaction mixture was acidified with sulfuric acid in the cold. About three-fourths of the solution was distilled; the distillate was saturated with potassium carbonate. The solution and oil was extracted with ether and dried over sodium sulfate. After removal of the ether the product was distilled through a short column giving 2.2 g. of crude ketone b. p. 58–65° (10 mm.). Redistillation gave 1.6 g. of 1,3-dimethoxyacetone b. p. 62.5–63° (10 mm.).

3-Methoxycyclohexanol.—Resorcinol (110 g.) was methylated at room temperature during two hours with dimethyl sulfate (100 ml.) in 600 ml. of water containing 100 g. of potassium hydroxide. The solution was acidified and extracted three times with benzene. The benzene solution was washed with 40 g. of sodium hydroxide in 600 ml. of water in three equal portions, in order to separate the desired product from the dimethylated material. The alkaline extract was acidified with hydrochloric acid, extracted with benzene, the solution dried, and the benzene distilled. Resorcinol monomethyl ether (59 g.) was distilled 115–119° (7.5 mm.). The product was hydrogenated over 5 g. of Raney nickel at 150° during forty-five minutes under 3000 p. s. i. of hydrogen. 3-Methoxycyclohexanol (36 g.) was obtained by fractionation of the product at 88–89° (8 mm.).

2- and 3-Methoxycyclohexanones.—These ketones were prepared by the oxidation of the corresponding alcohols, which had been prepared by hydrogenation of the corresponding phenols over Raney nickel as described for 3-methoxycyclohexanol. For example, 2-methoxycyclohexanol (28 g.) was added to a cool solution of 43 g. of potassium dichromate in 31 ml. of concentrated sulfuric acid and 190 ml. of water. The temperature rose from 12 to 65° and then slowly dropped to room temperature. The solution was extracted with 600 ml. of ether in three portions. The ether solution was washed with a carbonate solution and dried over sodium sulfate. Fractionation of the product gave 13 g. of 2-methoxycyclohexanone b. p. 58–59° (8 mm.), $n^{25}D$ 1.4519. The yield of 3-methoxycyclohexanone (3.8 g.) b. p. 76.5–77° (9 mm.), from 3-methoxycyclohexanol (22 g.) was rather low.

Dibenzyl Ketone.—A solution of 155 g. of benzyl cyanide in 200 ml. of ether was added to a solution of benzylmagnesium chloride, prepared from 37.7 g. of magnesium and 196 g. of benzyl chloride in 750 ml. of ether. The mixture was refluxed for two hours and the addition product hydrolyzed in ice-water and then with dilute sulfuric acid. The crude ketone (48 g.) was distilled at 138–140° (3 mm.). The ketone solidified and was crystallized from petroleum ether (b. p. 40–60°) to give 32 g., m. p. 32.5–34°, and 25 g., m. p. 35° after recrystallization.

α-Tetrahydrofuryl Methyl Ketone.—Ethyl tetrahydrofuroate (b. p. 73–74° (11 mm.), $n^{25}D$ 1.4328) was prepared by the hydrogenation of ethyl furoate (220 g.) over Raney nickel at 100° in 88% yield. Ethyl α-tetrahydrofuroylacetate was prepared through the reaction of the sodium salt of ethyl acetoacetate (0.63 mole) with ethyl tetrahydrofuroate (1.25 moles) at 150–155°, for four hours by the method of McElvain and Weber.[25] The desired keto ester 15.5 g., b. p. 115–116° (8 mm.), $n^{25}D$ 1.4530 was obtained by fractionation of the crude distillate. The keto ester (15 g.) was hydrolyzed in a 5% sodium hydroxide solution during four hours on a steam-bath. The cold solution was acidified with dilute sulfuric acid and two-thirds of the solution distilled. The distillate was made slightly alkaline and two-thirds of it again distilled. The distillate was saturated with potassium carbonate and extracted twice with ether. The ether solution was dried and the desired ketone (4.9 g., b. p. 160.5–161.5° (740 mm.)) distilled through a short Vigreux column.

Benzhydryl Methyl Ketone.—Lead diphenylacetate was prepared by the reaction of lead nitrate in a slightly acid water solution of sodium diphenylacetate. Dry lead diphenylacetate (31 g.) was intimately mixed with dry lead acetate (62 g.) in a mortar and the mixture heated under reduced pressure in a 250-ml. distilling flask held in a Woods metal bath at 280°. A yellow distillate (6 g.) was obtained and redistilled at 155–157° (8 mm.) to give 3.7 g. of crude ketone. The product solidified when kept overnight in a refrigerator, and was then crystallized from 40 ml. of petroleum ether (b. p. 40–60°). In different experiments both the stable form m. p. 58–60° and the unstable form m. p. 45–46° of the ketone were obtained in beautiful white crystals.[26,27]

Summary

The oxidation potentials of eighty-seven ketones and aldehydes have been determined by equilibrating them against each other and against three quinones of known oxidation potentials. The data are summarized in Table I. The limitations and reliability of the data and some of the relationships of structure to oxidation potentials have been discussed.

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(23) "Organic Syntheses," **13**, 74, John Wiley and Sons, Inc., New York, N. Y., 1933.

(24) Schreiner, *Ann.*, **197**, 8 (1879).

(25) McElvain and Weber, THIS JOURNAL, **63**, 2192 (1941).

(26) Kenner and Morton, *Ber.*, **72**, 452 (1939).

(27) Stoermer and Riebel, *ibid.*, **39**, 2302 (1906).