Carbohydrate Research, 146 (1986) 97–105
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

METAL-ION OXIDATION REACTIONS OF MONOSACCHARIDES: A KINETIC STUDY*

ANAND G. FADNIS[†]
Department of Chemistry, Government Post Graduate College, Mhow-453441 MP (India)

(Received July 17th, 1984; accepted for publication in revised form, May 1st, 1985)

ABSTRACT

The kinetics of oxidation of hexoses, pentoses hexitols, and a pentitol by vanadium(V), cerium(IV), manganese(III), and thallium(III) in aqueous acidic media are best explained by a free-radical mechanism. Oxidation reactions of alditols produces the corresponding aldoses, which are further oxidised in the presence of an excess of oxidant to lower monosaccharides and thence to formaldehyde, formic acid, and even to carbon dioxide. All of the reactions except that of thallium(III) are acid-catalysed. Other kinetic data are summarised and the rate laws are given.

INTRODUCTION

Metal-ion oxidants have been widely employed in synthetic chemistry[1–3] including carbohydrate chemistry[4–7]. These are stable, inexpensive, and can readily be stored and handled. This paper presents a summary of the oxidation reactions of certain metal ions with monosaccharides. The oxidants used were vanadium(V)[8,9], cerium(IV)[10,11], manganese(III)[12,13], and thallium(III)[14]. The monosaccharides employed included hexoses (D-glucose, D-mannose, D-galactose, D-fructose, L-sorbose, and L-rhamnose), pentoses (D-xylose, D-arabinose, and D-ribose), hexitols (D-mannitol, D-glucitol, and D-galactitol), and a pentitol (ribitol). The mode of investigation was mainly kinetic. Other relevant supporting data were also obtained.

EXPERIMENTAL

Materials. — Commercially available chemicals of pure quality were used without further purifications. Stock solutions of monosaccharides (BDH Biochemical, BDH/AR) were prepared fresh in double-distilled water. Vanadium(V), cerium(IV), and thallium(III) stock-solutions were prepared by dissolving ammonium metavanadate (Reidel, Germany), ceric sulphate (E. Merck), and thallic

---

*Presented at the XIIth International Carbohydrate Symposium, Utrecht, The Netherlands, 1–7 July, 1984.

[†] Mailing address: 191 Palsikar Colony, Indore-452004, MP, India.

0008-6215/86/$ 03.50

oxide (BDH/AR), respectively, in aqueous sulphuric, hydrochloric, or perchloric acids. The manganese(III) stock-solution was prepared by the procedure described in the literature[15].

Kinetic methods. — The kinetic runs were performed in stoppered glass vessels in a controlled-temperature (±0.1°) water-bath. The reactions were monitored titrimetrically by determining the concentration of unused oxidant in the presence of excess concentrations (~10–20 fold) of monosaccharide and acid. Vanadium(V), cerium(IV), and manganese(III) were estimated by quenching the aliquots in an excess of Fe(II) solution and then determining unreacted Fe(II) with a previously standardised solution of ceric sulphate, with *N*-phenyl anthranilic acid as indicator[8-13]. Thallium(III) was estimated iodometrically[14].

RESULTS AND DISCUSSION

(a) *Monosaccharide in excess.* — Under the kinetic-run conditions, one mol of monosaccharide consumed ~2 equivalents of vanadium(V), cerium(IV), and manganese(III), and ~1 equivalent of thallium(III). In the reactions with hexitols, the corresponding aldohexoses, and in the reactions of the aldohexoses and the pentitol, the corresponding aldopentoses, were confirmed as products by paper chromatography and other conventional tests.

The stoichiometric reactions may therefore be represented as in Eq. *1–3*.

$$\mathrm{C_6H_{14}O_6 + 2V(V)/Ce(IV)/Mn(III) \rightarrow C_6H_{12}O_6 + 2V(IV)/Ce(III)/Mn(II) + 2H^+} \tag{1}$$

$$\mathrm{C_6H_{12}O_6 + 2V(V)/Ce(IV)/Mn(III) \rightarrow C_5H_{10}O_5 + HCO_2H + 2V(IV)/Ce(III)/Mn(II) + 2H^+} \tag{2}$$

$$\mathrm{C_6H_{12}O_6 + Tl(III) \rightarrow C_5H_{10}O_5 + HCO_2H + Tl(I) + 2H^+} \tag{3}$$

Formic acid was also estimated quantitatively, and the results confirmed[14b] the Eq. *3*. Aldotetroses were also confirmed as products of the oxidation reactions of the aldopentoses.

(b) *Oxidant in excess*. When the oxidant is present in large excess (~20 fold), the monosaccharide molecule is oxidised to formaldehyde, formic acid, and even to carbon dioxide. The stoichiometric equations, on the basis of equivalents of oxidant consumed per mol of monosaccharide under various experimental conditions, may be given as in Eq. *4–11*.

$$\mathrm{C_6H_{14}O_6 + 14V(V)/Ce(IV) + 6H_2O \rightarrow 6HCO_2H + 14V(IV)/Ce(III) + 14H^+} \tag{4}$$

$$\mathrm{C_6H_{14}O_6 + 8Mn(III) + 3H_2O \rightarrow 3HCO_2H + 3HCHO + 8Mn(II) + 8H^+} \tag{5}$$

$$\mathrm{C_6H_{12}O_6 + 12Tl(III) + 6H_2O \rightarrow 6CO_2 + 12Tl(I) + 24H^+} \tag{6}$$

$$\mathrm{C_6H_{12}O_5 + 5Tl(III) + 5H_2O \rightarrow 4HCO_2H + 2HCHO + 5Tl(I) + 10H^+} \tag{7}$$

$$\mathrm{C_5H_{12}O_5 + 12V(V)/Ce(IV) + 5H_2O \rightarrow 5HCO_2H + 12V(IV)/Ce(III) + 12H^+} \tag{8}$$

$$\mathrm{C_5H_{12}O_5 + 6Mn(III) + 2H_2O \rightarrow 2HCO_2H + 3HCHO + 6Mn(II) + 6H^+} \tag{9}$$

$$\mathrm{C_5H_{10}O_5 + 10V(V) + 5H_2O \rightarrow 5HCO_2H + 10V(IV)/Ce(III) + 10H^+} \tag{10}$$

$$\mathrm{C_5H_{10}O_5 + 6Mn(III) + 3H_2O \rightarrow 3HCO_2H + 2HCHO + 6Mn(II) + 6H^+} \tag{11}$$

The formation of free radicals during these reactions (*1–11*) was confirmed by the polymerization reaction induced with acrylonitrile.

Kinetic studies. — (a) *Variation in concentrations of oxidant and monosaccharide.* The disappearance of oxidant with time uniformly followed first-order kinetics in each run. The values of the pseudo-first-order rate-constants, $k_{obs}(sec^{-1})$, at different initial concentrations of oxidant were generally found constant, with some exceptions.

However, the rate constant (k_{obs}, sec^{-1}) increased as a function of increase in the concentration of monosaccharide. The order with respect to substrate is unity in all of the reactions except those of vanadium(V), cerium(IV), and manganese(III) with hexitols, manganese(III) with pentoses, and thallium(III) with ketohexoses. In these reactions, the formation constants of the complexes (K) and their rates of disproportionation (k_s) were determined from Michaelis–Menten plots (Table I).

(b) *Variations in concentration of acid.* —The rate of oxidation by vanadium(V) and manganese(III) increased with acid (sulphuric–hydrochloric–perchloric) concentration, whereas the rate of oxidation by cerium(IV) and thallium(III) decreased with sulphuric and perchloric acids, respectively. The rate of oxidation by vanadium(V), cerium(IV), and manganese(III) increased with H^+ concentration, whereas a decrease in rate was observed in reactions with thallium(III), and the rate of vanadium(V) reaction with alditols remained unchanged. However, the dependence of rate constant on acid–H^+ concentrations was found different in the individual classes of reactions, according to the type and the concentration-range of the acid used.

Certain criteria following Zücker and Hammett[16], Bunnett[17], and Bunnett and Olsen[18] were applied to the rate data. The involvement of a water molecule as the proton-transferring agent has been suggested on the basis of values of the "w" and ϕ parameters[17,18] computed in all of the reactions. Furthermore, the ϕ values,

TABLE I

COMPLEX FORMATION-CONSTANTS (K) AND RATE CONSTANTS FOR COMPLEX DISPROPORTIONATION (k_s)

Monosaccharide	$K \times 10^{-3} L.mol^{-1}$				$k_s \times 10^4 sec^{-1}$			
	V(V)	*Ce(IV)*	*Mn(III)*	*Tl(III)*	*V(V)*	*Ce(IV)*	*Mn(III)*	*Tl(III)*
D-Mannitol	2.94	0.96	4.53		0.50	100.0	5.88	
D-Glucitol	1.25	8.80	4.95		0.01	31 25	125.00	
D-Galactitol	7.77	0.99	3.05		0.07	125.00	47.00	
D-Fructose				0 35				14.28
L-Sorbose				0.08				32.25
D-Xylose			0.03				32.15	
D-Arabinose			1.02				38.18	
D-Ribose			0.87				25.23	

which characterise the kinetic response of the reaction to changing concentration of the acid was used to calculate the specific rate of the reactions[8c,14b].

(c) *Reactive species of oxidants.* — These have been proposed on the basis of rate data obtained by the variation of acid, hydrogen-ion concentration and its conjugate-anion concentration. Vanadium(V) exists as the yellow pervanadyl ion VO_2^+ in aqueous acidic medium, but this form may change with the acid used and its concentration-range used in a particular reaction[19]. The following equilibria have been considered in proposing the reactive species in the present reactions studied in different acid-media[8,9].

Perchlorid acid

$$VO_2^+ + H_3O \rightleftharpoons V(OH)_3^{2+} \tag{12}$$
$$VO_2^+ + 2H^+ \rightleftharpoons V(OH)_2^{3+} \tag{13}$$

Sulphuric acid

$$VO_2^+ + H_3O^+ + HSO_4^- \rightleftharpoons [V(OH)_3HSO_4]^+ \tag{14}$$
$$VO_2^+ + 2H^+ + 2HSO_4^- \rightleftharpoons [V(OH)_2(HSO_4)_2]^+ \tag{15}$$
$$(VO_2 \cdot 2H_2O)^+ + 2H_2SO_4 \rightleftharpoons (VO_22HSO_4)^+ + 2H_2O \tag{16}$$

Hydrochloric acid

$$VO_2^+ + H_3O^+ + Cl^- \rightleftharpoons [V(OH)_3Cl]^+ \tag{17}$$

Cerium(IV) exists in various forms in sulphuric acid[20]. $Ce(SO_4)_2$ has been considered as the reactive species, and the kinetic data have been accounted by considering the following equilibria[10,11].

$$Ce(SO_4)_2 + HSO_4^- \rightleftharpoons HCe(SO_4)_3^- \tag{18}$$
$$Ce(SO_4)_2 + SO_4^{2-} \rightleftharpoons Ce(SO_4)_3^{2-} \tag{19}$$
$$Ce(SO_4)_2 + H_2SO_4 \rightleftharpoons H_2Ce(SO_4)_3 \rightleftharpoons 2H^+ + Ce(SO_4)_3^{2-} \tag{20}$$

Manganese(III) has been described[21] as $Mn(H_2P_2O_7)_3^{3-}$ in the pH range 0–3. In the present reactions, the increase in rate $[H^+]$ may be explained by considering the change in active species, as[13] in Eq. *21*.

$$Mn(H_2P_2O_7)_3^{3-} + H^+ \rightleftharpoons Mn(H_3P_2O_7)(H_2P_2O_7)_2^{2-} \tag{21}$$

In oxidation reactions by thallium(III), the inverse dependence of rate on $[H^+]$ has been explained by considering $Tl(OH)_2^+$ as the reactive species[14].

$$Tl^{3+} + H_2O \rightleftharpoons Tl(OH)_2^{2+} \rightleftharpoons H^+ \tag{22}$$

TABLE II

THERMODYNAMIC PARAMETERS

Monosaccharide	$\Delta H^{\ddagger}$ *kJ mol*$^{-1}$				$\Delta S^{\ddagger}$ *deg*$^{-1}$ *mol*$^{-1}$			
	V(V)	*Ce(IV)*	*Mn(III)*	*Tl(III)*	*V(V)*	*Ce(IV)*	*Mn(III)*	*Tl(III)*
D-Mannitol	88.90 ±0.58	135.76 ±0.33	109.30 ±1.62		−59.27 ±5.01	104.40 ±6.48	20.44 ±4.97	
D-Glucitol	94.12 ±2.10	138.73 ±0.58	81.09 ±0.37		−36.71 ±1.23	136.30 ±0.12	33.12 ±0.17	
D-Galactitol	103.74 ±2.14	113.15 ±0.29	93.80 ±3.75		34.90 ±6.06	52.16 ±0.16	34.56 ±0.16	
D-Glucose				119.13 ±0.21				24.57 ±0.08
D-Galactose				119.27 ±0.25				40.48 ±0.16
D-Mannose				121.01 ±0.29				43.91 ±0.08
D-Fructose				134.11 ±0.37				86.33 ±0.71
L-Sorbose	88.42 ±9.39			103.06 ±0.71	28.89 ±1.23			39.58 ±0.12
L-Rhamnose				137.81 ±0.12				89.63 ±0.04
Ribitol	83.31 ±0.16	100.19 ±0.04	95.72 ±0.20		93.25 ±0.16	1.29 ±0.20	34.77 ±0.20	
D-Xylose	89.86 ±0.17	91.69 ±0.36	73.69 ±0.62		−27.76 ±0.13	−5.99 ±0.38	−42.28 ±0.63	
D-Arabinose	95.46 ±0.32	80.23 ±0.21	78.36 ±0.57		−10.21 ±0.31	−8.83 ±0.41	−25.36 ±0.26	
D-Ribose	87.04 ±0.36	83.15 ±0.36	73.12 ±0.68		−33.66 ±0.33	−15.23 ±0.62	−20.31 ±0.18	

TABLE III

CORRELATION OF PERCENT OF FREE ALDEHYDE FROM AND k_0 ($dm^3\ mol^{-1}sec^{-1}$) OF DIFFERENT ALDOSES[a]

Aldose		D-*Glucose*	D-*Mannose*	D-*Galactose*	D-*Xylose*	D-*Arabinose*	D-*Ribose (0.1*M*)*
(Free Aldehyde) (%)		0.024	0.064	0.085	0.170	0.280	8.5
$k_0 \times 10^4 dm^3$	*A*	0.28	0.32	1.81	5.31	6.93	9.72
	B	4.18	7.38	10.21	17.8	20.32	25.28
$mol^{-1}sec^{-1}$	*C*	6.39	14.81	16.30	25.7	30.32	36.31
	D	2.18	10.42	24.53	22.34	42.30	48.19

[a](*A*) [V(V)] = 0.01M, [Aldose] = 0.1M, $[H_2SO_4]$ = 3.5M, Temp. = 40°;
(*B*) [Ce(IV)] = 0.01M, [Aldose] = 0.1M, $[H_2SO_4]$ = 4.0M, Temp. 30°;
(*C*) [Mn(III)] = 0.005M, [Aldose] = 0.1M, $[H_2SO_4]$ = 1.0M, $[H_2P_2O_7^{2-}]$ Free = 0.053M, Temp. = 25°;
(*D*) [Tl(III)] = 0.01M, [Aldose] = 0.2M, $[HClO_4]$ = 1.0M, Temp. = 65°.

(d) *Variation in temperature.* Kinetic data have been obtained at different temperatures for the reactions. The thermodynamic parameters were computed from Arrhenius plots and are given in Table II.

(e) *Correlation of rate and configuration.* — Monosaccharides have both acyclic and cyclic forms that exist in dynamic equilibria. The rate of mutarotation of D-glucose has been determined as 0.42 sec^{-1} at 70° and $[H^+] = 0.68$M from the reported rate values, the equilibrium constant, and the activation energy for mutarotation of glucose[22,23]. The rate of oxidation of D-glucose with thallium(III) is determined to be $0.04 \times 10^{-4} sec^{-1}$ from the experimental pseudo-first-order rate constants, k_{obs} $0.79 \times 10^{-4} sec^{-1}$, under the same conditions. This value for the rate of oxidation is very small compared to the rate of mutarotation, and thus it may be assumed that the oxidation rate is not affected by mutarotation and is the sum of the rates contributed by α, β, and free-aldehyde forms.

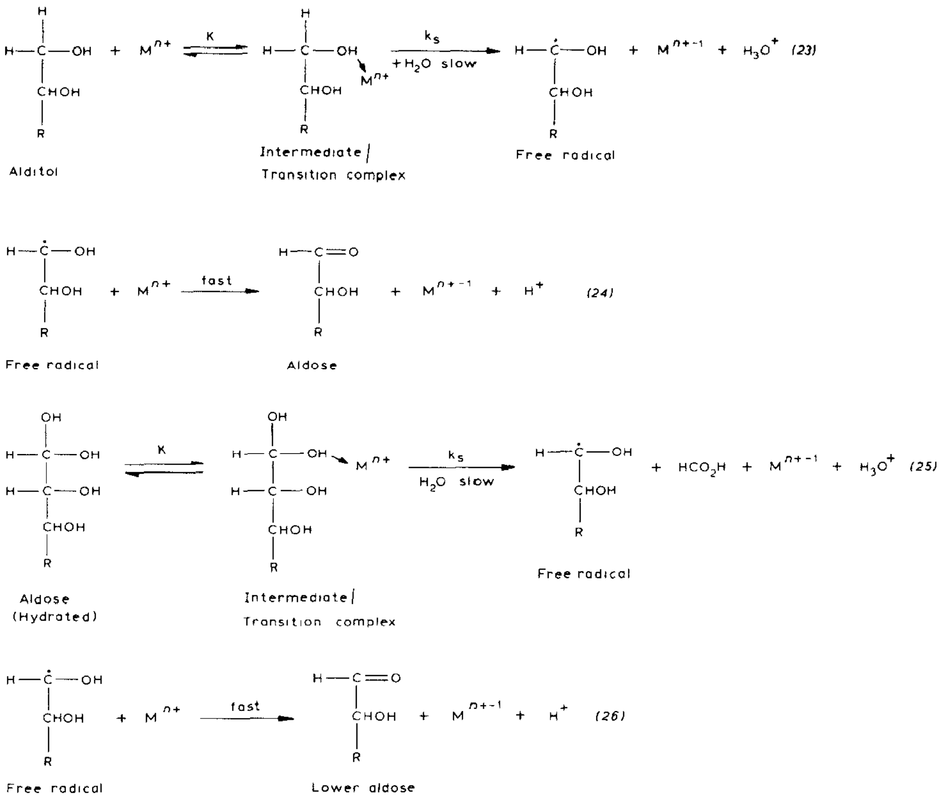
A linear relation has been observed between the second-order rate constant, k_o, for various aldoses and their percentages of aldehyde form[24,25]. This relation clearly explains that most of the monosaccharides (aldoses) are oxidised through their acyclic forms, as the percentages of their α and β anomers are almost the same. This linear relationship also explains the observed reactivity of different aldoses (Table III), which is in the order: D-ribose > D-arabinose > D-xylose > D-galactose > D-mannose > D-glucose.

Mechanistic steps. — A general mechanism for all of these reactions may now be proposed on the basis of results obtained during stoichiometric and kinetic studies. It is obvious that there is an interaction between oxidant and substrate resulting in electron transfer between them. Kinetic evidence shows that, in certain reactions (Table I), an intermediate complex is formed in a rapid, preliminary equilibrium step, which disproportionates unimolecularly in the rate-determining step. In reactions where there is no kinetic evidence for complex formation, it may be assumed either that the electron transfer takes place in the transition state or an intermediate complex of low stability is formed. Although the kinetic features of all of these reactions are different, a general mechanistic scheme may be proposed that depicts the general behaviour of monosaccharides toward these metal-ion oxidants (Scheme I).

In the presence of an excess of oxidant, the sequence continues, and formaldehyde, formic acid, and even carbon dioxide are obtained in fast steps by a free-radical mechanism.

Thallium(III) is a two-equivalent oxidant and may be changed to thallium(I) in either a single step[26,27] or in two successive, one-electron steps with a thallium(II) intermediate. Formation of a free radical supports the possibility of two successive, one-electron changes in thallium(III).

Oxidation reactions by manganese(III) are ligand-displacement reactions in which a diphosphate ligand is displaced by a monosaccharide molecule and a cyclic complex is formed. This hypothesis is supported by the observed retardation of the rate of oxidation by an increase in the concentration of free diphosphate[12,13]



Scheme I

Rate laws. — From the proposed steps *23* and *24*, or *25* and *26* in Scheme I, the general rate-law may be derived as:

$$-\mathrm{d}\frac{[\mathrm{M}^{n+}]}{\mathrm{d}t} = \frac{K\,k_s\,[\text{monosaccharide}][\mathrm{M}^{n+}]}{1 + K[\text{monosaccharide}]}$$

$$= k_{\text{obs}}\,[\mathrm{M}^{n+}] \qquad (27)$$

Thus

$$k_{\text{obs}} = \frac{K\,k_s\,[\text{monosaccharide}]}{1 + K[\text{monosaccharide}]} \qquad (28)$$

Michaelis–Menten plots have been drawn between $1/k_{\text{obs}}$ and 1/[monosaccharide], and the values of the formation constant of the complex (K) and the rate constant of its disproportion (k_s) have been determined (Table I).

In order reactions where there is no kinetic evidence for the formation of a complex. K should be very small.

Hence

$$-\mathrm{d}\frac{[\mathrm{M}^{n+}]}{\mathrm{d}t} = K\,k_{\mathrm{s}}\,[\text{monosaccharide}][\mathrm{M}^{n+}]$$

$$= k_{\mathrm{obs}}\,[\mathrm{M}^{n+}] \qquad (29)$$

For a particular reaction, the additional steps for the formation of reactive species (Eqs. *12–21*) may be considered and the general rate-law (Eq. *28* and *29*) modified accordingly.

REFERENCES

1 R. L. AUGUSTINE, *Oxidation,* Vols. I and II, Marcel Dekker, New York, 1969.

2 L. J. CHINN, *Selection of Oxidants in Synthesis: Oxidation at Carbon Atoms,* Marcel Dekker, New York, 1971.

3 B. S. TYAGRAJAN, *Selective Organic Transformation,* Vol. 12, Wiley–Interscience, New York, 1972.

4 W. L. EVANS, *Chem. Rev.,* 6 (1929) 281–300.

5 R. F. BUTTERWORTH AND S. HANESSIAN, *Synthesis,* (1971) 70–88.

6 K. HEYNS AND H. PAULSEN, *Adv. Carbohydr. Chem.,* 17 (1962) 169–172.

7 (a) R. D. GUTHRIE, *Adv. Carbohydr. Chem.,* 17 (1962) 105–108; (b) H. O. TSELOK, *Synthesis,* (1973) 347–363.

8 (a) R. P. BHATNAGAR AND A. G. FADNIS, *J. Indian Chem. Soc.,* 53 (1976) 999–1001; 55 (1978) 357–361; (b) *idem, Monatsh. Chem.,* 111 (1980) 927–933; (c) *idem, Gazz. Chim. Ital.,* 110 (1980) 479–482.

9 (a) A. G. FADNIS AND S. K. KULSHTRESTHA, *J. Indian Chem. Soc.,* 58 (1981) 763–765; 59 (1982) 411–413; (b) *idem, Cienc. Cult. (Sao Paulo),* 34 (1982) 209–212; (c) *idem, Z. Phys. Chem. (Leipzig),* 263 (1982) 1060–1064.

10 R. P. BHATNAGAR AND A. G. FADNIS, *Cienc. Cult. (Sao Paulo),* 30 (1978) 1227–1230.

11 A. G. FADNIS AND S. K. KULSHTRESTHA, *Rev. Roum. Chem.,* 28 (1983) 99–103.

12 R. P. BHATNAGAR AND A. G. FADNIS, *Monatsh. Chem.,* 109 (1978) 319–323.

13 (a) A. G. FADNIS AND S. K. KULSHTRESTHA, *React. Kinet. Catal. Lett. (Hungary),* 19 (1982) 267–269; (b) *idem, Carbohydr. Res.,* 112 (1983) 137–140.

14 A. G. FADNIS AND S. K. SHRIVASTAVA, *Natl. Acad. Sci. Lett. (Allahabad, India),* 3 (1980) 85–87; (b) *idem, Carbohydr. Res.,* 102 (1982) 23–29; (c) *idem, J. Indian Chem. Soc.,* 60 (1983) 147–149; (d) *idem, Cienc. Cult. (Sao Paolo),* 33 (1981) 1335–1337.

15 J. J. LINGANGE AND R. KARPLUS, *Ind. Eng. Chem.,* 18 (1946) 191–195.

16 L. ZUCKER AND L. R. HAMMETT, *J. Am. Chem. Soc.,* 69 (1939) 2775–2784.

17 J. F. BUNNETT, *J. Am. Chem. Soc.,* 83 (1961) 4956 and succeeding papers, pp. 4958–4867.

18 J. F. BUNNETT AND F. P. OLSEN, *Can. J. Chem.,* 44 (1966) 1899–1916.

19 H. C. MISHRA AND M. C. R. SYMONS, *J. Chem. Soc.,* (1962) 1411–1415.

20 T. J. HARDWICK AND E. ROBERTSON, *Can. J. Chem.,* 29 (1951) 828–834.

21 I. M. KOLTHOFF AND J. I. WATTERS, *J. Am. Chem. Soc.,* 70 (1948) 2455–2459.

22 R. P. BELL, *Acid Base Catalysis,* Clarendon Press, Oxford, 1941, pp. 65–66.

23 E. A. MOELWYN-HUGHES, *The Kinetics of Reaction in Solution,* Don Press, Oxford, 1950, p. 67.

24 S. M. CANTOR AND Q. P. PENISTON, *J. Am. Chem. Soc.,* 62 (1940) 2113–2121.

25 M. RUDRUM AND D. F. SHAW, *J. Chem. Soc.,* (1965) 52–57.

26 H. N. HALVORSON AND J. HALPERN, *J. Am. Chem. Soc.,* 78 (1958) 5562–5566.

27 J. HALPERN AND S. M. TAYLOR, *Discuss. Faraday Soc.,* 29 (1960) 1174–1181.