

Oxidation of D-glucose by Cu(II) in acidic medium [†]

Sandra Signorella, Rubén Lafarga, Laura Ciullo, Luis F. Sala *

*Area Inorgánica, Departamento de Química Física, Universidad de Rosario,
Suipacha 531 (2000) Rosario, Argentina*

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Abstract

The oxidation of D-glucose by Cu(II) has been studied in NaAcO buffers within the pH range of 4–5 at 110°C. The observed pseudo-first-order rate constant is given by: $a[\text{AcO}^-] + b/[\text{H}^+] + c[\text{AcO}^-][\text{Glc}] + d[\text{Glc}]/[\text{H}^+]^2$, where $a = 5.3 \pm 0.4 \times 10^{-4} \text{ s}^{-1} \text{ M}^{-1}$, $b = 1.30 \pm 0.07 \times 10^{-8} \text{ s}^{-1} \text{ M}$, $c = 6.16 \pm 0.04 \times 10^{-3} \text{ s}^{-1} \text{ M}^{-2}$, and $d = 3.2 \pm 0.2 \times 10^{-13} \text{ s}^{-1} \text{ M}$. This rate law corresponds to the formation of gluconic acid and Cu(I) when a ten-fold or higher excess of D-glucose over Cu(II) is employed. The results are discussed in terms of a possible mechanism of oxidation of D-glucose by CuOAc^+ , present in solution.

1. Introduction

It is well known that Cu(II) oxidizes reducing sugars in strongly alkaline medium [1–4]. Under alkaline conditions, the oxidation rate has been found to be zero-order in Cu(II) and the sugar enolization rate is the limiting step. No detailed kinetic studies have been undertaken in acidic medium. Oxidation of aldoses by CuSO_4 at pH 1.0 and temperatures between 100–130°C was reported by Kuprenskii [5]. These results, however could not be reproduced in our laboratory. The present paper deals with the kinetics of oxidation of D-glucose by Cu(II) at the minimum pH range where the reaction takes place.

2. Experimental

Kinetics experiments.—The reaction mixtures were prepared by mixing $\text{Cu}(\text{ClO}_4)_2$ (Fluka grade) in appropriate solutions of NaOAc–AcOH and variable amounts of

* Corresponding author.

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D-glucose (Sigma grade) in order to obtain the desired relationship [oxidant–reductant]. Ionic strength was kept at $I = 0.59$ M throughout the experiment employing sodium perchlorate (Fluka grade). Oxygen was purged from the solutions by bubbling N_2 through the solutions protected by serum caps. Residual dioxygen in the N_2 was removed by passing the N_2 through scrubbers containing pyrogallol. All solutions were prepared with deionized water which had been distilled from alkaline permanganate in a glass apparatus. The sealed solutions were brought to the desired temperature within 15 s using an electrically regulated thermostat. A set of 20 ampoules for each D-glucose/Cu(II) ratio was prepared. The reaction was quenched by quickly cooling the solutions. The Cu_2O produced in the reaction was filtered off and 50% NH_4OH was added to the filtrate. Unreacted Cu(II) was determined spectrophotometrically as the $Cu(NH_3)_4^{2+}$ complex ($\lambda_{max} = 620$ nm, $\epsilon = 42$ M $^{-1}$ cm $^{-1}$) on a Shimadzu UV-140 double beam spectrophotometer. The nature of the precipitate was confirmed by treating it with HCl in the presence of glycerin to stabilize Cu(I), thereby avoiding its dismutation to Cu(II) and Cu(0). The complete dissolution of the precipitate confirms the formation of Cu_2O and the absence of Cu(0). A large excess of D-glucose (10 to 100 fold) was used for all kinetic measurements. Pseudo-first-order rate constants were determined from the slope of $\ln[Cu(II)]$ vs. time plots. All the rate constants are the average of three determinations at each set of conditions.

The pH was checked with a Chemcadet pH meter calibrated against standard NBS buffer solution provided by the Cole–Parmer Instrument Company at temperatures between 70 and 95°C; pH values at 110°C were obtained by extrapolation. No changes in pH values were observed with temperature.

Product analysis.—Qualitative identification of carbohydrate oxidation products was carried out by paper chromatography using 4:1:5 *n*-butanol–AcOH–H $_2$ O as eluent. Paper chromatograms were visualized by two development reagents, silver nitrate/NaOH/Na $_2$ S $_2$ O $_3$ [6] and β -naphthol–sulfanilamide [7], specific for aldonic acid detection. In this way, D-gluconic acid was identified by comparison with an authentic sample as the only oxidation product, either when an excess of oxidant or organic substrate was employed. The stoichiometry of the reaction was found to be 2 Cu(II) per mol of sugar.

Detection of free radicals.—A solution of $Cu(ClO_4)_2$ (5 mL, 0.01 M) was added to a mixture of D-glucose (0.05 mmol) and acrylonitrile (0.03 mol) to a final volume of 7 mL. The reaction was allowed to go to completion at 110°C as judged by the change in color of the solution. A white gel appeared slowly. Blank experiments in the absence of D-glucose or Cu(II) did not show gel formation.

3. Results and discussion

The minimum pH at which the reaction takes place at a temperature above 100°C was found to be 4.0 instead of pH 1.0 as reported by Kuprenskii [5] at the same temperature (Fig. 1a). At pH 4.75 no reaction was observed below 100°C (Fig. 1b).

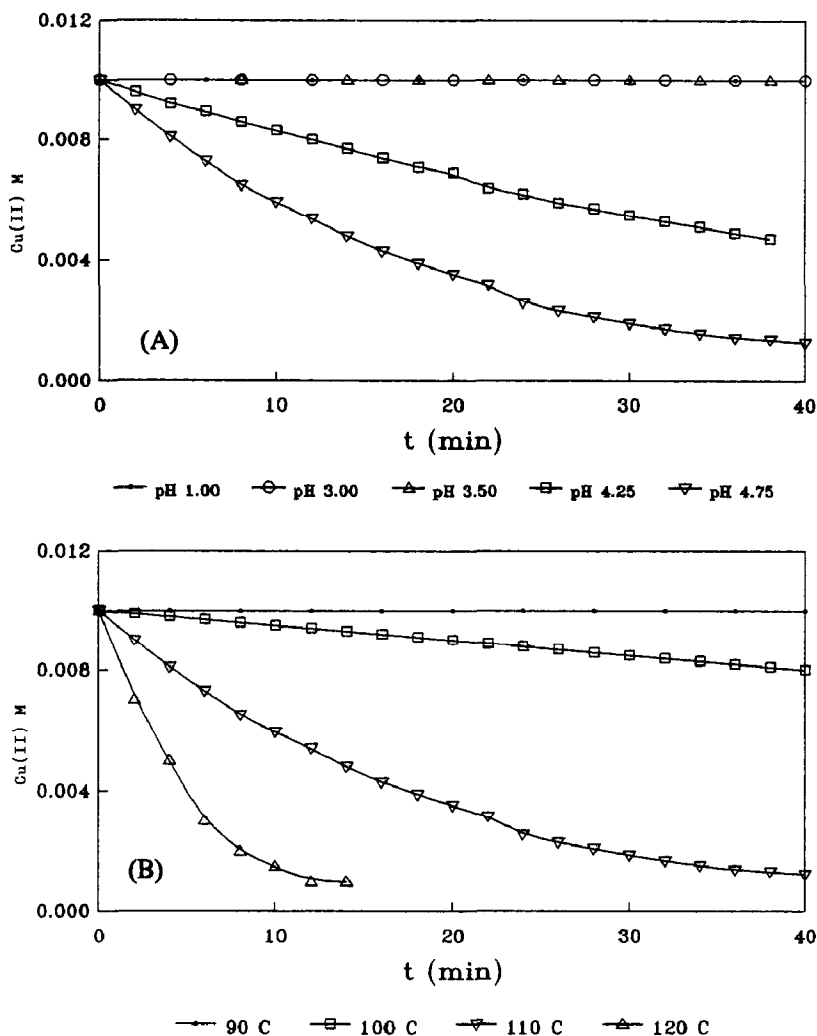


Fig. 1. Concentration vs. time curves for Cu(II) oxidation of D-glucose. (A) at different pH, temperature, 110°C, [Glc], 0.1 M; (B) different temperatures, [Glc], 0.1 M, pH 4.75.

Within the range of concentrations of this study, no precipitate of cupric hydroxide was produced by mixing the reactants at pH 4–5, and the reaction mixture was perfectly homogeneous before the reaction started. However, it did not remain homogeneous throughout because of the formation of cuprous oxide as a heterogeneous reaction product during the kinetic runs. No autocatalysis by cuprous oxide was observed. This was confirmed by adding Cu_2O to the mixture without any change in the experimental data.

When oxygen was not removed from the solution, oxidation started after a slight induction period, which was practically eliminated when N_2 was bubbled through

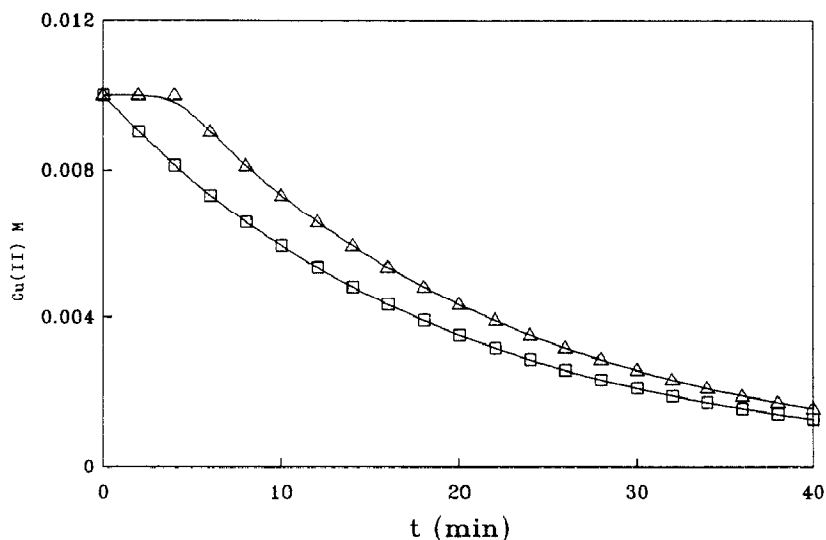


Fig. 2. Oxygen influence on the oxidation rate, [Glc], 0.1 M; temperature, 110°C; pH, 4.75.

before the reaction was initiated (Fig. 2). The pseudo-first-order oxidation rate (k_{obsd}) was studied as a function of the concentration of D-glucose (0.1–0.9 M) and hydrogen ion (1×10^{-5} – 1×10^{-4} M) at 110°C (Table 1).

Table 1

Observed and calculated pseudo-first-order rate constants for different acidities ^a

	pH 4.00					
[Glc] (M)	0.1	0.2	0.3	0.5	0.7	0.9
$k_{\text{obsd}} \times 10^4$ (s ⁻¹)	2.15	2.45	2.80	4.00	4.75	5.37
$k_{\text{calcd}} \times 10^4$ (s ⁻¹)	1.98	2.35	2.73	3.48	4.24	5.00
	pH 4.25					
[Glc] (M)	0.1	0.2	0.3	0.5	0.7	0.9
$k_{\text{obsd}} \times 10^4$ (s ⁻¹)	3.10	3.95	3.70	5.10	5.65	—
$k_{\text{calcd}} \times 10^4$ (s ⁻¹)	3.06	3.51	3.95	4.84	5.74	6.63
	pH 4.50					
[Glc] (M)	0.1	0.2	0.3	0.5	0.7	0.9
$k_{\text{obsd}} \times 10^4$ (s ⁻¹)	4.60	5.60	6.00	6.90	8.60	10.0
$k_{\text{calcd}} \times 10^4$ (s ⁻¹)	5.07	5.74	6.41	7.74	9.07	10.4
	pH 4.60					
[Glc] (M)	0.1	0.2	0.3	0.5	0.7	0.9
$k_{\text{obsd}} \times 10^4$ (s ⁻¹)	—	7.00	8.10	10.3	10.9	13.3
$k_{\text{calcd}} \times 10^4$ (s ⁻¹)	6.33	7.18	8.04	9.74	11.4	13.2
	pH 4.75					
[Glc] (M)	0.1	0.2	0.3	0.5	0.7	0.9
$k_{\text{obsd}} \times 10^4$ (s ⁻¹)	8.70	10.3	12.9	14.9	16.6	20.5
$k_{\text{calcd}} \times 10^4$ (s ⁻¹)	8.96	10.3	11.7	14.4	17.1	19.8

^a Temperature, 110°C; [AcO⁻], 0.056 M; *I*, 0.59.

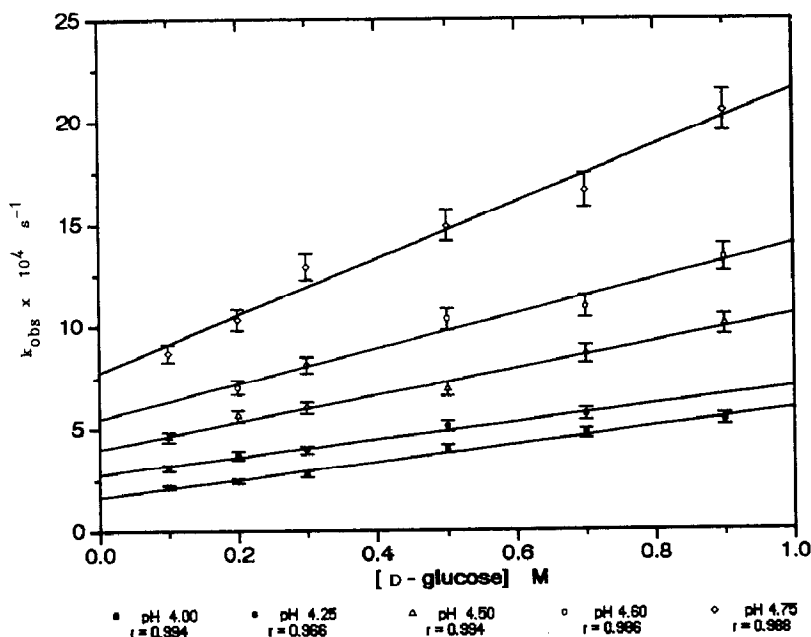


Fig. 3. k_{obs} as a function of D-glucose concentration at different acidities, temperature, 110°C; $[\text{AcO}^-]$, 0.056 M; $[\text{Cu(II)}]$, 0.01 M; I , 0.59.

At five different acidities and constant acetate concentration, plots of k_{obsd} vs. D-glucose (Glc) concentration gave good straight lines with a positive intercept (Fig. 3) from which values of k_1 and k_2 were determined (Table 2).

Plots of k_1 vs. $1/[\text{H}^+]$ and k_2 vs. $1/[\text{H}^+]^2$ gave straight lines described by Eqs. 1 and 2:

$$k_1 = A + B/[\text{H}^+] \quad (1)$$

$$k_2 = C + D/[\text{H}^+]^2 \quad (2)$$

where $A = 3 \times 10^{-5} \text{ s}^{-1}$, $B = 1.3 \times 10^{-8} \text{ s}^{-1} \text{ M}$, $C = 3.45 \times 10^{-4} \text{ s}^{-1} \text{ M}^{-1}$, and $D = 3.20 \times 10^{-13} \text{ s}^{-1} \text{ M}$.

The reaction was also studied by varying $[\text{AcO}^-]$ at fixed $[\text{H}^+]$ or $[\text{AcO}^-]/[\text{AcOH}]$ ratios and $[\text{Glc}] = 0.2 \text{ M}$ (Table 3). Plots of k_{obsd} vs. $[\text{AcO}^-]$ gave

Table 2

Values of k_1 and k_2 as a function of pH determined from the y-intercepts in Fig. 3

pH	4.00	4.25	4.50	4.60	4.75
$k_1 \times 10^4 (\text{s}^{-1})$	1.67	2.79	4.03	5.53	7.76
$k_2 \times 10^4 (\text{s}^{-1} \text{ M}^{-1})$	4.25	4.20	6.49	8.41	13.8

Table 3

Observed pseudo-first-order rate constants for different $[\text{AcO}^-]$ at four fixed pH values ^a

pH	$[\text{AcO}^-] \times 10^2 \text{ (M)}$	$k_{\text{obsd}} \times 10^4 \text{ (s}^{-1}\text{)}$
4.25	1.92	2.90
	2.46	3.10
	4.26	3.40
	5.60	3.90
	10.0	4.70
4.50	2.52	4.90
	3.58	5.40
	5.60	5.60
	6.72	6.00
	10.0	6.80
4.75	4.00	9.90
	5.60	10.3
	8.96	10.9
	11.0	11.3
	15.0	12.2
5.00	5.80	19.2
	7.97	19.7
	9.97	20.0
	12.0	20.5

^a Temperature, 110°C; $[\text{Cu(II)}]$, 0.01 M; $[\text{Glc}]$, 0.2 M; I , 0.59.

straight lines with practically the same slope and different positive intercepts described by Eq. 3:

$$k_{\text{obsd}} = E + F[\text{AcO}^-] \quad (3)$$

where $F = 2.2 \pm 0.2 \times 10^{-4} \text{ s}^{-1} \text{ M}^{-1}$. The dependence of E on $[\text{H}^+]$ was found to be:

$$E = G/[\text{H}^+] + H/[\text{H}^+]^2 \quad (4)$$

where $G = 1.31 \pm 0.05 \times 10^{-10} \text{ s}^{-1} \text{ M}$ and $H = 4.7 \pm 1.5 \times 10^{-14} \text{ s}^{-1} \text{ M}^2$. Values of E and F are listed in Table 4.

Correlation of values of constants obtained from data in Tables 1 and 3, shows that: $B = G$, $D [\text{Glc}] = H$, and $A + C [\text{Glc}] = F [\text{AcO}^-]$. In this way, the deduced rate law is given by:

$$-(d[\text{Cu(II)}]/dt) = k_{\text{obsd}}[\text{Cu(II)}] = \{a[\text{AcO}^-] + b/[\text{H}^+] + c[\text{Glc}][\text{AcO}^-] + d[\text{Glc}]/[\text{H}^+]^2\}[\text{Cu(II)}] \quad (5)$$

Table 4

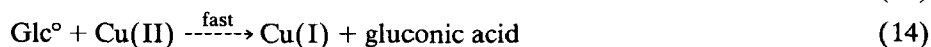
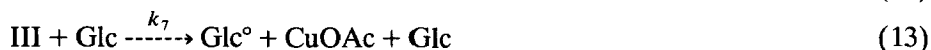
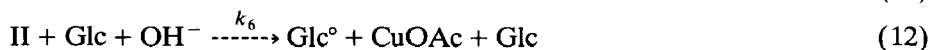
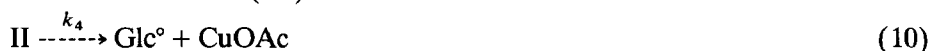
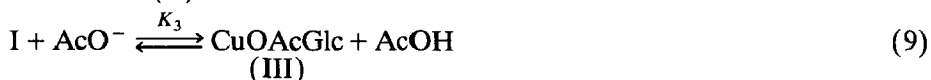
Values of E and F as a function of pH calculated using Eqs. 3 and 4

pH	4.25	4.50	4.75	5.00
$E \times 10^4 \text{ (s}^{-1}\text{)}$	2.52	4.37	9.09	18.0
$F \times 10^4 \text{ (s}^{-1} \text{ M}^{-1}\text{)}$	2.22	2.41	2.04	2.05

where $a = 5.3 \pm 0.4 \times 10^{-4} \text{ s}^{-1} \text{ M}^{-1}$, $b = 1.30 \pm 0.07 \times 10^{-8} \text{ s}^{-1} \text{ M}$, $c = 6.16 \pm 0.04 \times 10^{-3} \text{ s}^{-1} \text{ M}^{-2}$, and $d = 3.2 \pm 0.2 \times 10^{-13} \text{ s}^{-1} \text{ M}$. These values of a , b , c , and d were used to find k_{calcd} in Table 1, which are in excellent agreement with experimental data over the concentration range studied.

Before dealing with the mechanism, the distribution of species in the reaction in the system will be considered. Many hydrolysed Cu(II) species of the general form $\text{Cu}_m(\text{OH})_n^{(2m-n)+}$ are known [8,9]. However, under our experimental conditions, dissolved copper exists mainly as CuOAc^+ [10,11] and binuclear copper complexes, which are formed at pH values greater than those used here [12,13] will be disregarded. Further, in acetate buffer, CuOAc^+ has been reported to be an active species in oxidation reactions [14].

On the other hand, acids are far less effective catalysts than alkalis for the enolization of sugars, and glucose shows its maximum stability under acid conditions [15]. UV absorption bands characteristic of enediols ($\lambda_{\text{max}} = 312 \text{ nm}$ [16]) in acetate-buffered glucose used in the kinetic measurements were not observed after heating at 110°C . This finding means that enediol is either formed but reacts too rapidly to be detected or it is not formed. For the sake of simplicity and since enediol was not observed, it is not considered in the mechanism discussed below. The possibility of glucose isomerization after heating at 110°C in the pH range 4–5 was also evaluated. Paper chromatography of these glucose solutions did not show any isomer formation, as compared with authentic samples. The stability of glucose under our experimental conditions was confirmed by specific rotation measurements, which demonstrated that no glucose decomposition occurred. Finally, after the kinetics experiments, the unreacted glucose was determined by the glucose oxidase assay [17]. The quantitative recovery of glucose confirmed that glucose is neither isomerised nor decomposed under the conditions used in this work.



Scheme 1.

In accordance with the experimental data, we propose the mechanism shown in Scheme 1. In this mechanism, glucose binds CuOAc^+ to form complex I. This complex is in equilibrium with II and III, which might be formulated as copper–acetate–glucose complexes from which a proton has been removed, presumably from Cu(II) -bound water (in II) or from a hydroxyl group on glucose (in III). Complexes II and III lead to the dissociation of a glucose radical from Cu(I) through an intramolecular electron transfer process (Eqs. 10 and 11, a second molecule of glucose (Eq. 13), or a base catalyzed path (Eq. 12). If it is assumed that eqs. 6–9 involve rapidly established equilibria, then the pseudo-first-order rate constant in the scheme is given by Eq. 15.

$$\begin{aligned}
 & -\frac{d[\text{Cu(II)}]}{dt} \\
 & = k_{\text{obsd}}[\text{Cu(II)}] \\
 & = \left(\frac{k_4 K_2}{[\text{H}^+]} + k_5 K_3 [\text{AcO}^-] + k_6 K_2 K_w \frac{[\text{Glc}]}{[\text{H}^+]^2} \right. \\
 & \quad \left. + k_7 K_3 [\text{Glc}] [\text{AcO}^-] K_{1\text{AcO}^-} [\text{Glc}] [\text{AcO}^-] [\text{Cu(II)}] K_1 \right) \\
 & \quad \times \left(1 + K_{1\text{AcO}^-} [\text{AcO}^-] + K_1 K_{1\text{AcO}^-} [\text{Glc}] [\text{AcO}^-] \right. \\
 & \quad \left. + K_{1\text{AcO}^-} K_1 K_2 \frac{[\text{AcO}^-]}{[\text{H}^+]} [\text{Glc}] + K_1 K_{1\text{AcO}^-} \frac{K_3 [\text{AcO}^-]^2 [\text{Glc}]}{[\text{AcOH}]} \right)^{-1} \quad (15)
 \end{aligned}$$

Glucose provides OH^- groups for metal binding which enables the formation of complexes with ions and, although Cu(II) is a soft cation, it binds polyhydroxylic compounds to yield complexes with large formation constants [13,14], indicating that K_1 should be large. On the contrary, the hydrolysis constants, K_2 and K_3 , are expected to be $\ll K_1$. Thus, under our experimental conditions, it seems reasonable that $K_1 K_{1\text{AcO}^-} [\text{Glc}] [\text{AcO}^-]$ should be the largest term in the denominator and Eq. 15 will be simplified to the experimentally observed form.

Polymerization after addition of acrylonitrile supports the formation of glucose radicals. These radicals are formed in the slow steps and may rapidly react with Cu(II) to yield Cu(I) and gluconic acid as final products (Eq. 14). The above analysis explains the absence of D-glucose oxidation by Cu(II) at high $[\text{H}^+]$ and, although Cu(II) itself is not an active species when coordinated to acetate, it is able to oxidize D-glucose to gluconic acid. In this way, it seems that anions reduce the barrier to transform Cu(II) to Cu(I) .

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