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Article

Degradation of Ampicillin and Flucloxacillin Antibiotics via Oxidation by Alkaline Hexacyanoferrate(III): Kinetics and Mechanistic Aspects

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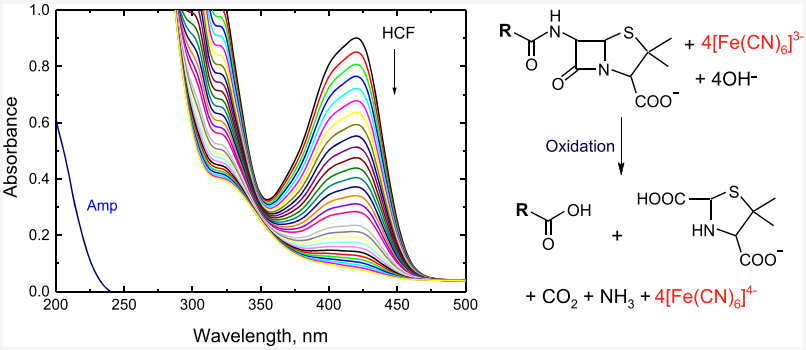

ABSTRACT: The kinetics and mechanistic aspects of the oxidation of two beta-lactam antibiotics (A), ampicillin and flucloxacillin, by alkaline hexacyanoferrate(III) (HCF(III)) were examined using spectrophotometry at a fixed temperature. The oxidation reactions showed a 1:4 (A: HCF(III)) stoichiometry. The reaction kinetics were found to follow first-order dependence for the oxidant and fractional first-order dependence for [A] and [OH^-]. The enhancement of the ionic strength and dielectric constant was found to increase the oxidation rates. Free radical tests of the reactions showed positive results. The addition of HCF(II) as a predicted oxidation product did not considerably change the oxidation rates. Under the same experimental conditions, the oxidation rate of ampicillin was found to be slightly lower than that of flucloxacillin. The acquired oxidation products were recognized using spot testing and Fourier transform infrared spectra. A conceivable oxidation mechanism was suggested. A derived rate law expression was found to be consistent with the experimental results. The activation parameters were assessed and discussed.

INTRODUCTION

Antibiotics, or antibacterials, are very significant drugs that are utilized for treating infections in humans, animals, and plants.[1] Although antibiotics are essentially required for humans, they are foreign matters to the body and must be removed after playing their medicinal action through a process called drug metabolism that is carried out in the liver. In drug metabolism, antibiotics undergo oxidation, reduction, hydrolysis, and so forth, resulting in biotransformation of antibiotics in the body so that they can be removed more easily. This process may lead to a pharmacologically active, inactive, or toxic metabolite, which is excreted into the environment.[2−6] Because antibiotics contain complex organic compounds in their structures that they can transform biologically into other components and may persist in the environment for prolonged periods without degradation, they can be considered a serious pollution factor in the environment;[7−10] antibiotics can also have toxic and negative impacts and disrupt the ecological balance. Thus, there is a great need to identify effective green treatment techniques for the removal of such residues to protect the environment and human health.[11−17] Unfortunately, normal biological treatment methods do not satisfy all requirements for degradation because of complicated antibiotic structures.[18] Therefore, improved methods must be employed.[18−21]

Antibiotics are generally liable to oxidation, resulting in their degradation and the termination of their action and/or their removal from the body.[22−29] Therefore, one of the most favorable ways to achieve the decomposition of antibiotics is a treatment process resulting in their oxidation.[22−29] Through such a process, oxidants may alter toxic compounds to less harmful ones, leading to their safe discharge to the environment.[28,29] An accurate literature survey illuminates little detailed kinetic studies for the oxidative degradation of antibiotics in an aqueous medium and/or such studies provide

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poor mechanistic information.[24−29] The present investigation aims to provide a mechanistic picture for the biotransformation of antibiotics in the body as well as understanding how oxidation of certain functional groups in these organic molecules can affect antibiotic actions. In view of the forgoing aspects, the kinetics and mechanistic aspects of the oxidative degradation of two significant beta-lactam antibiotics, ampicillin and flucloxacillin, were investigated using hexacyanoferrate(III) (HCF(III)) as an efficient oxidant in an alkaline medium.[30−38]

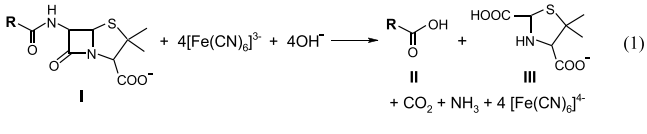
EXPERIMENTAL SECTION

Materials. The chemicals utilized in this study were purchased from Sigma or Merck, and double-distilled water was utilized in the preparation of their solutions. Stock solutions of ampicillin and flucloxacillin were freshly prepared by dissolving the prerequisite weights for the samples (ampicillin and flucloxacillin sodium salts, Glentham Life Sciences) in double-distilled water. A fresh solution of the oxidant was prepared in double-distilled water and was standardized using spectrophotometry. Solutions of NaOH and $NaClO_4$ were used to preserve and examine the influence of the pH and ionic strength (I) of the reaction medium, respectively. *Tert*-butanol was utilized to identify the influence of the dielectric constant (D) of the reaction medium.

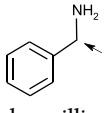
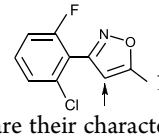
Kinetic Measurements. Kinetic experiments were carried out under isolated conditions; that is, the antibiotic concentration was in excess than that of HCF(III). All experiments were carried out at a fixed ionic strength and temperature. The absorbance spectra were acquired using a UV−vis double-beam spectrophotometer (Shimadzu UV-1800). The kinetics of the reactions were monitored by recording the decay in HCF(III) absorbance versus time at λ_{max} = 420 nm. At least two freelance kinetic runs were carried out, and the experimental outcomes showed a reproducibility of approximately ±4%.

RESULTS AND DISCUSSION

Stoichiometry of the Oxidation Reactions and Product Identification. The stoichiometry of the present reactions in an alkaline medium was examined utilizing spectrophotometry at λ = 420 nm. The median $\Delta[A]/\Delta[HCF(III)]$ ratio at constant $[OH^-]$ and ionic strength (I) was determined to be 1:4. The experimental outcomes revealed that 4 mol of HCF(III) was expended by 1 mol of the antibiotic, as presented by the following equationwhere **R**



I II III (1)

=  for ampicillin and **R** =  for flucloxacillin, and compounds **II** and **III** are their characterized oxidation products, the corresponding carboxylic acids and 5,5-dimethyl-thiazolidine-2,4-dicarboxylic acid, respectively. The products acquired from oxidation were characterized using spot testing and Fourier transform infrared (FT-IR) spectra. As a representative example, the FT-IR spectra for both ampicillin and its acquired oxidation products are shown in the Supporting Information in Figure S1a,b, respectively. A broad band is observed at 3371 cm^{-1} in Figure S1b due to carboxylic OH with N−H stretching, which is in accordance with product **III**. The same figure shows vanishing of the absorption band at 1770 cm^{-1} (for the amidic ketone C═O stretch) in the ampicillin spectrum, Figure 1a. Furthermore,

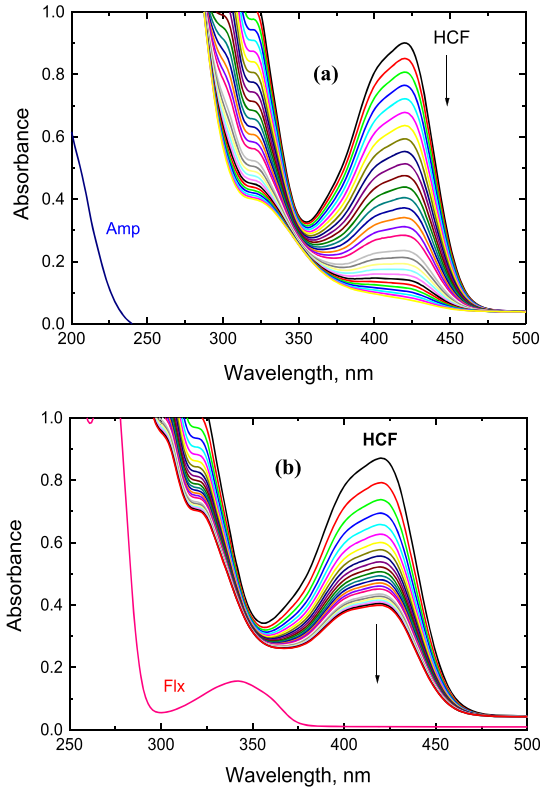


Figure 1. UV−vis spectra measured throughout the oxidation of (a) ampicillin (Amp) and (b) flucloxacillin (Flx) antibiotics by alkaline HCF(III). $[A] = 3.0 \times 10^{-2}$ mol dm^{-3}, $[HCF(III)] = 7.0 \times 10^{-4}$ mol dm^{-3}, $[OH^-] = 3.0 \times 10^{-2}$ mol dm^{-3}, and I = 0.1 mol dm^{-3} at 298 K.

the sharp band is manifested at 1659 cm^{-1} due to carboxylic C═O stretching. The byproducts, ammonium ion and CO_2, were specified by spot tests.[39] The same oxidation products of ampicillin[27,28] and flucloxacillin[29] have been characterized previously.

Spectral Changes. The spectral differences observed during the oxidation of ampicillin (Amp) and flucloxacillin (Flx) antibiotics by alkaline HCF(III) are presented in Figure 1a,b, respectively. The registered spectra in this figure show a steady decay of the HCF(III) band at λ = 420 nm as the reactions advance because of its reduction by antibiotic molecules. This decay occurring during the oxidation of ampicillin was found to be slightly lower than that obtained for flucloxacillin oxidation under the same conditions.

Dependence of Oxidation Rates on the HCF(III) Concentration. The influence of $[HCF(III)]$ on the rate of oxidation of ampicillin and flucloxacillin antibiotics in an alkaline medium was explored by changing the HCF(III) concentration while $[A]$ and $[OH^-]$ remained fixed. The acquired plots of ln absorbance versus time were found to be linear, as shown in Figure 2 (for ampicillin as an example), with no noteworthy differences observed in the slopes of such plots (constancy of the first-order rate constant values, k_{obs}) at several $[HCF(III)]$ levels, as recorded in Table 1. Such

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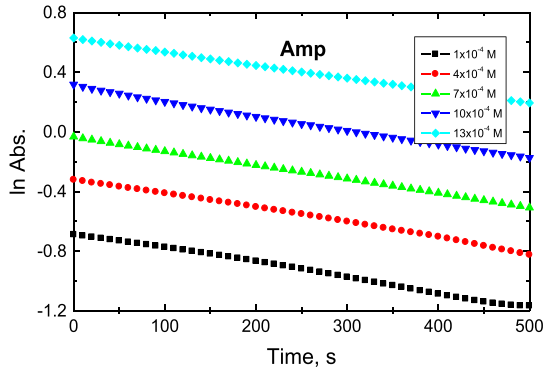

Figure 2. ln absorbance vs time graphs at several [HCF(III)] levels during the oxidation of ampicillin (Amp) by alkaline HCF(III). [Amp] = 3.0×10^{-2} mol dm^{-3}, [OH$^-$] = 3.0×10^{-2} mol dm^{-3}, and I = 0.1 mol dm^{-3} at 298 K.

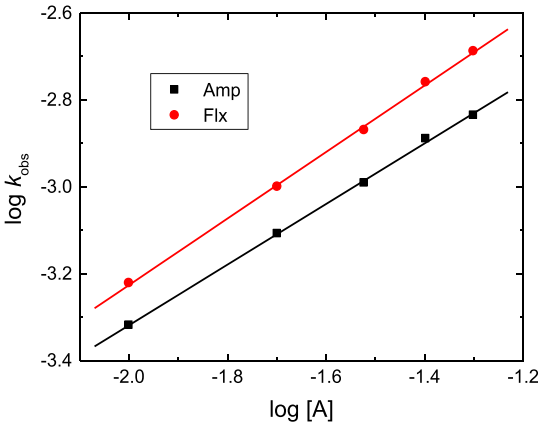

Figure 3. Graphs of log k_{obs} vs log [A] during the oxidation of ampicillin and flucloxacillin antibiotics by alkaline HCF(III). [HCF(III)] = 7.0×10^{-4} mol dm^{-3}, [OH$^-$] = 3.0×10^{-2} mol dm^{-3}, and I = 0.1 mol dm^{-3} at 298 K.

outcomes showed that the order with reference to [HCF(III)] was unity.

Dependence of Oxidation Rates on Antibiotic Concentration. For both the examined antibiotics, the oxidation rates were investigated at varying concentrations of antibiotics, $[A]_0$, with all other reactant concentrations fixed. The acquired results showed that the rates of oxidation in the reactions increased as the concentration of antibiotics increased, as noted from the values of k_{obs} given in Table 1. The graphs of k_{obs} versus [A], Figure S2 (Supporting Information), show good straight lines with positive intercepts on the k_{obs} axes. Furthermore, as illustrated in Figure 3, when the log [A] values were plotted against the log k_{obs} values, straight lines with slopes of 0.70 and 0.77 were obtained for ampicillin and flucloxacillin, respectively, indicating that the order of the reactions with regard to $[A]_0$ was fractional-first.

Dependence of Oxidation Rates on OH$^-$ Concentration. The hydroxyl-ion concentration was changed from 0.01 to 0.05 mol dm^{-3} while keeping all other conditions fixed. The results obtained showed that as [OH$^-$] increased, the rates of the reactions also increased (Table 1). The plots of k_{obs} versus [OH$^-$] (Figure S3 in the Supporting Information) showed straight lines with positive intercepts on the k_{obs} axes, which suggested that the orders of the reactions in [OH$^-$] were less than unity. Furthermore, as illustrated in Figure 4, when the log [OH$^-$] values were plotted against the log k_{obs} values, straight lines with slopes of 0.55 and 0.78 were obtained for ampicillin and flucloxacillin, respectively, validating the fractional first-order dependence on the alkali concentration.

Dependence of the Oxidation Rates on the Ionic Strength and Dielectric Constant. The impact of the ionic strength of the reaction medium was explored for both ampicillin and flucloxacillin antibiotics at a fixed reactant concentration by varying the concentration of the Na_2SO_4

Table 1. Influence of [HCF(III)], [A], [OH$^-$], and I on the k_{obs} Values during the Oxidation of Ampicillin and Flucloxacillin by Alkaline HCF(III) at 298 K

				10^4 k_{obs} (s^{-1})	
10^4 [HCF(III)] (mol dm^{-3})	10^2 [A] (mol dm^{-3})	10^2 [OH$^-$] (mol dm^{-3})	I (mol dm^{-3})	Ampicillin	Flucloxacillin
1.0	3.0	3.0	0.1	10.4	13.8
4.0	3.0	3.0	0.1	10.1	13.4
7.0	3.0	3.0	0.1	10.2	13.5
10.0	3.0	3.0	0.1	10.4	13.7
13.0	3.0	3.0	0.1	10.1	13.7
7.0	**1.0**	3.0	0.1	4.8	5.9
7.0	**2.0**	3.0	0.1	7.8	9.9
7.0	**3.0**	3.0	0.1	10.2	13.5
7.0	**4.0**	3.0	0.1	12.9	17.4
7.0	**5.0**	3.0	0.1	16.2	20.4
7.0	3.0	**1.0**	0.1	4.2	7.5
7.0	3.0	**2.0**	0.1	7.0	11.2
7.0	3.0	**3.0**	0.1	10.2	13.5
7.0	3.0	**4.0**	0.1	12.5	15.8
7.0	3.0	**5.0**	0.1	14.5	18.2
7.0	3.0	3.0	**0.1**	10.2	13.5
7.0	3.0	3.0	**0.15**	12.5	15.2
7.0	3.0	3.0	**0.2**	14.7	16.6
7.0	3.0	3.0	**0.25**	17.6	18.3
7.0	3.0	3.0	**0.3**	20.2	19.8

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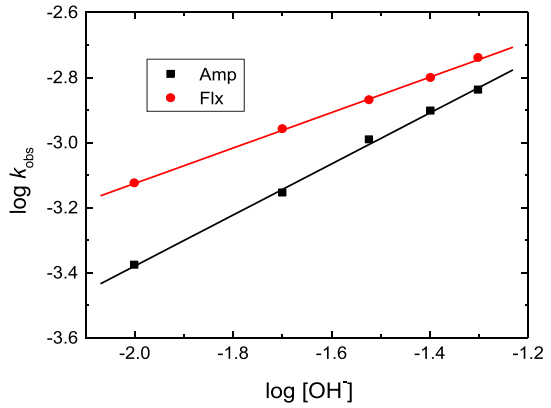

Figure 4. Graphs of log k_{obs} vs log [OH$^-$] during the oxidation of ampicillin and flucloxacillin antibiotics by alkaline HCF(III). [A] = 3.0×10^{-2} mol dm^{-3}, [HCF(III)] = 7.0×10^{-4} mol dm^{-3}, and I = 0.1 mol dm^{-3} at 298 K.

solution. The acquired results showed that with increasing ionic strength, the reaction rates decreased, as noticed from the values of k_{obs} recorded in Table 1. The Debye–Hückel graphs were found to be linear with positive slopes, as shown in Figure 5.

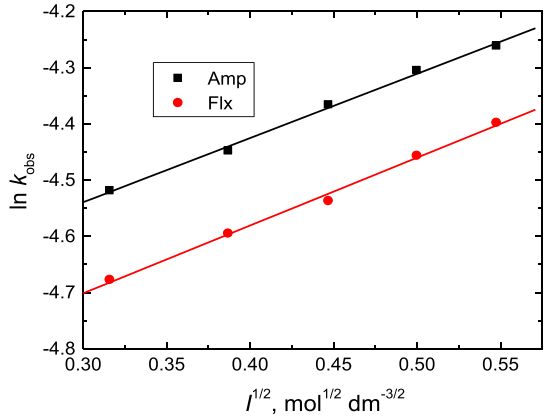

Figure 5. Debye–Hückel graphs during the oxidation of ampicillin and flucloxacillin antibiotics by alkaline HCF(III). [A] = 3.0×10^{-2} mol dm^{-3}, [HCF(III)] = 7.0×10^{-4} mol dm^{-3}, and [OH$^-$] = 3.0×10^{-2} mol dm^{-3} at 298 K.

To explore the consequence of the dielectric constant (D) of the reaction medium on reaction rates, the oxidation reactions for ampicillin and flucloxacillin antibiotics were explored at a variety of solvent percentages (vol %) of *tert*-butanol and water at stable reactant concentrations. The acquired outcomes revealed that k_{obs} decreased with an increasing *tert*-butanol percentage (i.e., a reduction in D), as shown in Table S1 (Supporting Information). The graphs of ln k_{obs} versus $1/D$ for both antibiotics were found to be linear with negative slopes, as illustrated in Figure 6.

Dependence of Oxidation Rates on the Initially Added Product, [HCF(II)]. The influence of the supplementation of various [HCF(II)] levels as a suggested product was examined (from 1.0×10^{-4} to 13.0×10^{-4} mol dm^{-3}) under fixed conditions for other constituents. The investigational outcomes verified that the addition of different concentrations of HCF(II) did not alter the oxidation rates, as shown in

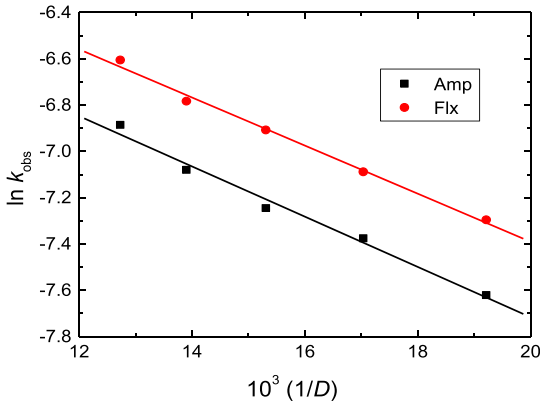

Figure 6. Graphs of ln k_{obs} vs $1/D$ during the oxidation of ampicillin and flucloxacillin antibiotics by alkaline HCF(III). [A] = 3.0×10^{-2} mol dm^{-3}, [HCF(III)] = 7.0×10^{-4} mol dm^{-3}, [OH$^-$] = 3.0×10^{-2} mol dm^{-3}, and I = 0.1 mol dm^{-3} at 298 K.

Figure S4 in the Supporting Information (for ampicillin as a representative example).

Dependence of Oxidation Rates on Temperature. The kinetics of the oxidation of ampicillin and flucloxacillin antibiotics by HCF(III) were studied at five different temperatures, from 288 to 328 K, with other conditions fixed. The obtained outcomes revealed that increasing temperature increased the rate of oxidation in the reactions, as shown by the values of k_{obs} recorded in Table S2 (Supporting Information). The activation parameters for the second-order rate constant, k_2, were calculated using Eyring and Arrhenius graphs (Figure 7a,b, respectively) and are listed in Table 2.

Test for Free Radicals. The sharing of free radical species during the oxidation of ampicillin and flucloxacillin antibiotics by HCF(III) was studied by the addition of definite acrylonitrile quantities to the reaction mixture under the conditions of an inert atmosphere for approximately 6 h. The formation of a heavy white precipitate indicated that the existing oxidation reactions proceeded via a mechanism involving free radicals.

Suggested Reaction Mechanism. The observed increase in the rate of oxidation in reactions with an increasing alkali concentration as well as the structures of the examined antibiotics suggests the deprotonation of antibiotic molecules (A) according to eq 2

$$A + OH^- \overset{K_1}{\rightleftharpoons} A^- + H_2O \quad (2)$$

Hence, the deprotonated form (A^-) may be regarded as a reactive species in the rate-controlling stage of the proposed reaction mechanism.

The oxidation of the antibiotics by alkaline HCF(III) shows a reaction stoichiometry of 4:1; that is, 4 mol of HCF(III) require 1 mol of the examined antibiotic. The reaction order for [HCF(III)] and [A] was first and fractional-first, respectively. As [OH$^-$] increases, the reaction rate also increases with a fractional first-order dependence, suggesting the deprotonation of antibiotics prior to the rate-controlling stage, as represented by eq 2. The oxidation rates increased as both I and D increased, suggesting that the existing oxidation reactions occurred between two ions with a similar charge sign,[40,41] that is, between A^- and $[Fe(CN)_6]^{3-}$ (HCF(III)). Additionally, the acquired fractional order regarding the

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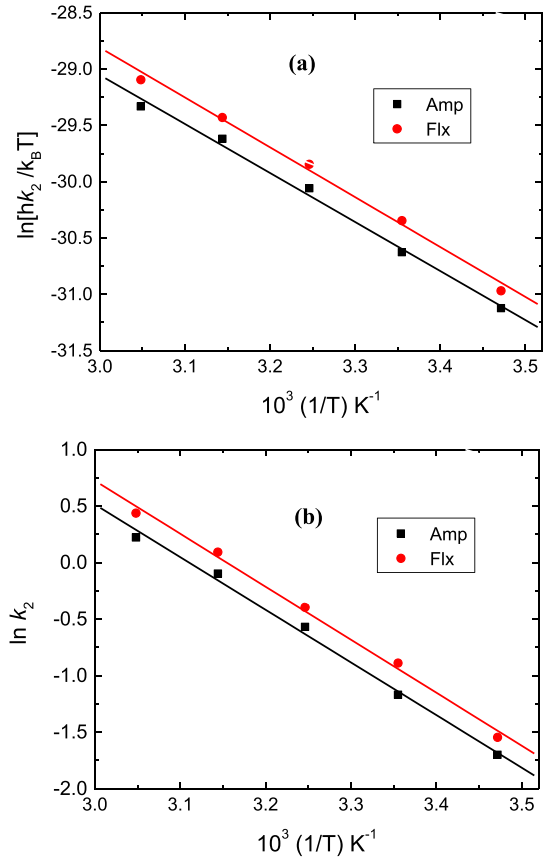

Figure 7. (a) Eyring graphs and (b) Arrhenius graphs of k_2 during the oxidation of ampicillin and flucloxacillin antibiotics by alkaline HCF(III). [A] = 3.0 × 10^{-2} mol dm^{-3}, [HCF(III)] = 7.0 × 10^{-4} mol dm^{-3}, [OH^-] = 3.0 × 10^{-2} mol dm^{-3}, and I = 0.1 mol dm^{-3}.

Table 2. Activation Parameters of k_2 during the Oxidation of Ampicillin and Flucloxacillin Antibiotics by Alkaline HCF(III)[a]

antibiotic	$\Delta S^{\ddagger}$ J mol^{-1} K^{-1}	$\Delta H^{\ddagger}$ kJ mol^{-1}	$\Delta G^{\ddagger}_{298}$ kJ mol^{-1}	$E_a^{\ddagger}$ kJ mol^{-1}
ampicillin	−133.0	36.0	75.6	38.7
flucloxacillin	−124.7	37.2	74.3	37.5

[a][A] = 3.0 × 10^{-2} mol dm^{-3}, [HCF(III)] = 7.0 × 10^{-4} mol dm^{-3}, [OH^-] = 3.0 × 10^{-2} mol dm^{-3} and I = 0.1 mol dm^{-3}.

antibiotics' concentration suggested the construction of a complex (C) between the two principal reacting species (A^- and $[Fe(CN)_6]3^-$).

In light of the acquired kinetic outcomes and product description, a conceivable oxidation reaction mechanism was hypothesized, involving the deprotonation of the antibiotic reductant to form a more reactive species. This is followed by the complexation of the deprotonated species with the oxidant to construct a complex (C), as exemplified by the following equation

$$A^- + [Fe(CN)_6]^{3-} \overset{K_1}{\rightleftharpoons} [A - Fe(CN)_5]^{3-}(C) + CN^- \quad (3)$$

Complex construction was also verified kinetically by the observation of positive intercepts in the graphs of $1/k_{obs}$ versus $1/[A]$,[42] as shown in Figure 8a. Then, the constructed intermediate complex (C) is gently decayed in the rate-

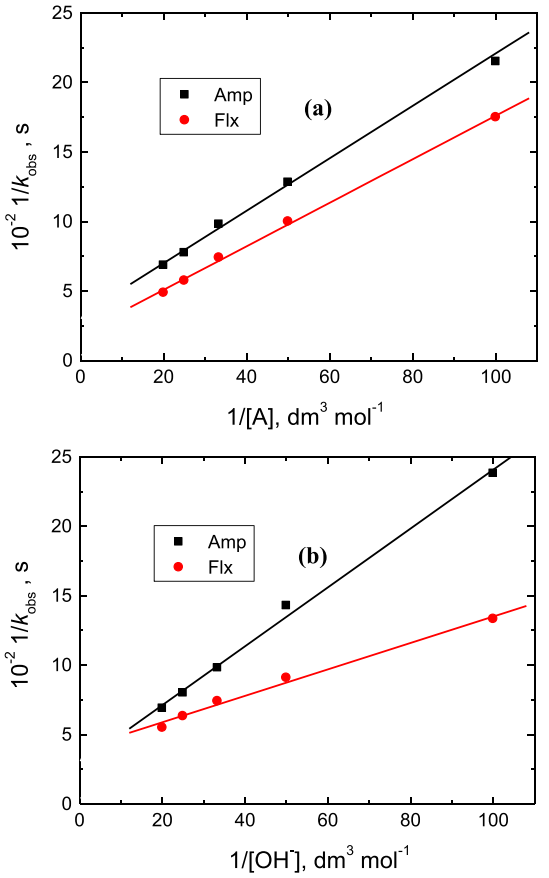

Figure 8. Verification of the derived rate law in the form of (a) eqs 8 and (b) 9 during the oxidation of ampicillin and flucloxacillin antibiotics by alkaline HCF(III). [HCF(III)] = 7.0 × 10^{-4} mol dm^{-3} and I = 0.1 mol dm^{-3} at T = 298 K.

controlling stage to yield an antibiotic free radical in addition to HCF(II), as represented by the following equation

$$[A - Fe(CN)_5]^{3-} \xrightarrow[\text{slow}]{K_1} A^{\cdot}(\text{free radical}) + [Fe(CN)_5]^{3-} \quad (4)$$

In subsequent fast stages, the antibiotic free radical reacts with other HCF(III) ions to form the final oxidation products, as elucidated in Scheme 1.

According to the proposed reaction mechanism, the rate law expressions were derived as follows (Appendix A in the Supporting Information)

$$\text{rate} = \frac{k_1K_1K_2[A][HCF(III)][OH^-]}{1 + K_1[OH^-] + K_1K_2[(III)H^-]} \quad (5)$$

Under isolated circumstances

$$\text{rate} = \frac{-d[HCF(III)]}{dt} = k_{obs}[HCF(III)] \quad (6)$$

Through the comparison of eqs 5 and 6, we can obtain the following equation

$$k_{obs} = \frac{k_1K_1K_2[A][OH^-]}{1 + K_1[OH^-] + K_1K_2[A][OH^-]} \quad (7)$$

By rearranging eq 7, the following relationships (8 and 9) can be obtained

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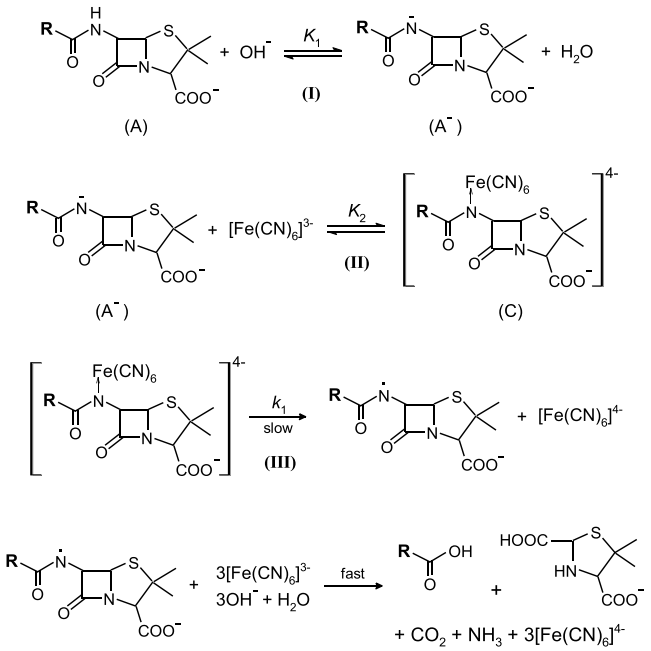
Scheme 1. Suggested Mechanism for the Oxidation of Ampicillin and Flucloxacillin Antibiotics by Alkaline HCF(III)



$$\frac{1}{k_{obs}} = \left(\frac{1}{k_1K_1K_2[OH^-]} + \frac{1}{k_1K_2}\right)\frac{1}{[A]} + \frac{1}{k_1} \quad (8)$$

$$\frac{1}{k_{obs}} = \left(\frac{1}{k_1K_1K_2[A]}\right)\frac{1}{[OH^-]} + \frac{1}{k_1K_2[A]}\frac{1}{k_1} \quad (9)$$

According to eqs 8 and 9, the graphs of $1/k_{obs}$ versus $1/[A]$ and $1k_{obs}$ versus $1/[OH^-]$ should be linear and were set to be so, as illustrated in Figure 8a,b, respectively. The values of the rate constants of the rate-controlling stage (k_1) and the equilibrium constants (K_1 and K_2) were computed from the slopes and intercepts of these graphs and are listed in Table 3.

Table 3. Values of k_1, K_1, and K_2 during the Oxidation of Ampicillin and Flucloxacillin Antibiotics by Alkaline HCF(III)[a]

	constant		
antibiotic	10^3 k_1, s^{-1}	K_1, dm^3mol^{-1}	K_2, dm^3mol^{-1}
ampicillin	3.19	1.84	295.17
flucloxacillin	5.13	20.61	32.18

[a] $[HCF(III)] = 7.0 \times 10^{-4}$ mol dm^{-3} and $I = 0.1$ mol dm^{-3} at $T = 298$ K

Activation Parameters. The acquired activation parameters given in Table 2 were set to be in good accord with the anticipated oxidation mechanism, where the high negative entropy of activation, $\Delta S^{\ddagger}$, specified the compression of the produced complexes (C).[43] The positive values of both enthalpy, $\Delta H^{\ddagger}$, and the free energy of activation, $\Delta G^{\ddagger}$, indicated that the formation of the complexes was endothermic and nonspontaneous, respectively. Additionally, the higher activation energy, $E_a^{\ddagger}$, indicates that the rate-controlling stage involved the decomposition of the constructed complexes.

CONCLUSIONS

1) The kinetics and mechanism of oxidation of ampicillin and flucloxacillin antibiotics by alkaline HCF(III) were explored.
2) Under the same experimental circumstances, the oxidation rate of ampicillin was found to be slightly lower than that obtained for flucloxacillin.
3) A conceivable oxidation mechanism was suggested.
4) A derived rate law expression was found to be consistent with the investigational outcomes.
5) The activation parameters were assessed and discussed.
6) The present study can be regarded as a promising treatment technique for the degradation of antibiotics to protect the environment and human health.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.iecr.0c03956.

FT-IR spectra of ampicillin and its oxidation products, plots of k_{obs} vs antibiotic concentration, plots of k_{obs} vs $[OH^-]$, plot illustrating the effect of [HCF(II)] on the oxidation of ampicillin by HCF(III), effect of dielectric constant and temperature on the values of k_{obs}, and derivation of the rate law expressions (PDF)

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Notes

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REFERENCES

(1) Schatz, A.; Bugle, E.; Waksman, S. A. Streptomycin, A Substance Exhibiting Antibiotic Activity against Gram-Positive and Gram-Negative Bacteria. *Exp. Biol. Med.* **1944**, *55*, 66.

(2) Gothwal, R.; Shashidhar, T. Antibiotic Pollution in the Environment: A Review. *Clean: Soil, Air, Water* **2005**, *43*, 479.
(3) Carvalho, I. T.; Santos, L. Antibiotics in the Aquatic Environments: A Review of the European Scenario. *Environ. Int.* **2016**, *94*, 736.
(4) Sanganyado, E.; Lu, Z.; Fu, Q.; Schlenk, D.; Gan, J. Chiral Pharmaceuticals: A Review on Their Environmental Occurrence and Fate Processes. *Water Res.* **2017**, *124*, 527.
(5) Brausch, J. M.; Connors, K. A.; Brooks, B. W.; Rand, G. M. Human pharmaceuticals in the aquatic environment: A review of recent toxicological studies and considerations for toxicity testing. *Rev. Environ. Contam. Toxicol.* **2012**, *218*, 1.
(6) Corcoran, J.; Winter, M. J.; Tyler, C. R. Pharmaceuticals in the Aquatic Environment: A Critical Review of the Evidence for Health Effects in Fish. *Crit. Rev. Toxicol.* **2010**, *40*, 287.
(7) Christou, A.; Agüera, A.; Bayona, J. M.; Cytryn, E.; Fotopoulos, V.; Lambropoulou, D.; Manaia, C. M.; Michael, C.; Revitt, M.; Schröder, P.; Fatta-Kassinos, D. The Potential Implications of Reclaimed Wastewater Reuse for Irrigation on the Agricultural Environment: The Knowns and Unknowns of the Fate of Antibiotics and Antibiotic Resistant Bacteria and Resistance Genes − A Review. *Water Res.* **2017**, *123*, 448.
(8) Sharma, V. K.; Johnson, N.; Cizmas, L.; McDonald, T. J.; Kim, H. A Review of the Influence of Treatment Strategies on Antibiotic Resistant Bacteria and Antibiotic Resistance Genes. *Chemosphere* **2016**, *150*, 702.
(9) Halling-Sørensen, B.; Nielsen, S. N.; Lankzky, P. F.; Ingerslev, F.; Lützhoft, H. C. H.; Jorgensen, S. E. Occurrence, Fate and Effects of Pharmaceutical Substances in the Environment. *Chemosphere* **1998**, *36*, 357.
(10) Kümmerer, K.; Al-Ahmad, A.; Mersch-Sundermann, V. Biodegradability of Some Antibiotics, Elimination of the Genotoxicity and Affection of Wastewater Bacteria in A Simple Test. *Chemosphere* **2000**, *40*, 701.
(11) Gurtekin, E.; Şekerdag, N. An Advanced Oxidation Process: Fenton Process. *Pamukkale Univ. J. Eng. Sci.* **2008**, *14*, 229.
(12) AL-Othman, Z. A.; Ali, R.; Naushad, M. Hexavalent Chromium Removal from Aqueous Medium by Activated Carbon Prepared from Peanut Shell: Adsorption Kinetics, Equilibrium and Thermodynamic Studies. *Chem. Eng. J.* **2012**, *184*, 238.
(13) Naushad, M. Surfactant Assisted Nano-Composite Cation Exchanger: Development, Characterization and Applications for the Removal of Toxic Pb2+ from Aqueous Medium. *Chem. Eng. J.* **2014**, *235*, 100.
(14) Naushad, M.; Ahamad, T.; Sharma, G.; Al-Muhtaseb, A. a. H.; Albadarin, A. B.; Alam, M. M.; ALOthman, Z. A.; Alshehri, S. M.; Ghfar, A. A. Synthesis and Characterization of A New Starch/SnO2 Nanocomposite for Efficient Adsorption of Toxic Hg2+ Metal Ion. *Chem. Eng. J.* **2016**, *300*, 306.
(15) Naushad, M.; Ahamad, T.; Al-Maswari, B. M.; Abdullah Alqadami, A.; Alshehri, S. M. Nickel Ferrite Bearing Nitrogen-Doped Mesoporous Carbon as Efficient Adsorbent for the Removal of Highly Toxic Metal Ion from Aqueous Medium. *Chem. Eng. J.* **2017**, *330*, 1351.
(16) Alqadami, A. A.; Naushad, M.; Alothman, Z. A.; Ghfar, A. A. Novel Metal−Organic Framework (MOF) Based Bomposite Material for the Sequestration of U(VI) and Th(IV) Metal Ions from Aqueous Environment. *ACS Appl. Mater. Interfaces* **2017**, *9*, 36026.
(17) Alqadami, A. A.; Naushad, M.; Abdalla, M. A.; Ahamad, T.; Abdullah ALOthman, Z.; Alshehri, S. M.; Ghfar, A. A. Efficient Removal of Toxic Metal Ions from Wastewater using a Recyclable Nanocomposite: A Study of Adsorption Parameters and Interaction Mechanism. *J. Clean. Prod.* **2017**, *156*, 426.
(18) Trovó, A. G.; Nogueira, R. F. P.; Agüera, A.; Fernandez-Alba, A. R.; Sirtori, C.; Malato, S. Degradation of Sulfamethoxazole in Water by Solar Photo-Fenton. Chemical and Toxicological Evaluation. *Water Res.* **2009**, *43*, 3922.
(19) Demirden, P. Treatability of Pharmaceutical Industry Wastewaters Containing Antibiotic in Anaerobic: Aerobic Sequential Processes, Ph.D. Thesis, Izmir, 2005.
(20) Ozkal, C. B.; Koruyucu, A.; Meric, S. Heterogeneous photocatalytic degradation, mineralization and detoxification of ampicillin under varying pH and incident photon flux conditions. *Desalin. Water Treat* **2016**, *57*, 18391. Garcıa, A. M.; Navarro, P. G.; Martınez, P. J.; de las, P. Degradation of Ampicillin in the Presence of Cadmium(II) Ions. *Talanta* **1998**, *46*, 101.
(21) Beltran, F. J. *Ozone Reaction Kinetics for Water and Wastewater Systems*; Lewis Publishers: Boca Raton, FL, 2003.
(22) Keen, O. S.; Linden, K. G. Degradation of Antibiotic Activity during UV/H2O2Advanced Oxidation and Photolysis in Wastewater Effluent. *Environ. Sci. Technol.* **2013**, *47*, 13020.
(23) Singh, A. K.; Singh, M.; Rahmani, S.; Srivastava, J.; Singh, J. Kinetics of the Oxidation of Tetracycline Hydrate by Copper(II) Complexed with Bipyridyl in Alkaline Medium using Chloro-Complex of Palladium(II) as Homogeneous Catalyst. *Ind. Eng. Chem. Res.* **2012**, *51*, 5728.
(24) Singh, A. K.; Negi, R.; Jain, B.; Katre, Y.; Singh, S. P.; Sharma, V. K. Kinetics and Mechanism of Ru(III)-Catalyzed Oxidation of Paracetamol by Chloramine-T in Aqueous Acidic Medium. *Catal. Lett.* **2009**, *132*, 285.
(25) Hosahalli, R. V.; Byadagi, K. S.; Nandibewoor, S. T.; Chimatadar, S. A. Kinetics and mechanism of ruthenium(III) catalyzed oxidation of chloromphenicol-An antibiotic drug by diperiodatocuprate(III) in aqueous alkaline medium. *Kinet. Catal.* **2012**, *53*, 65.
(26) Shetti, N. P.; Rajesh, N. H.; Nandibewoor, S. T. Structure Reactivity and Thermodynamic Analysis on the Oxidation of Ampicillin Drug by Copper(III) Complex in Aqueous Alkaline Medium (Stopped-Flow Technique). *J. Mol. Struct.* **2009**, *930*, 180.
(27) Singh, A. K.; Yadav, R.; Srivastava, J.; Bala, R. S.; Pradhan, R.; Rahmani, S. Kinetics of Ir(III)-Catalysed Oxidation of Ampicillin by $Cu(Bip)_2^{2+}$ in Alkaline Medium: A Spectrophotometric Study. *Int. J. ChemTech Res.* **2017**, *10*, 514.
(28) Hosamani, R. R.; Shetti, N. P.; Nandibewoor, S. T. Mechanistic Investigation on the Oxidation of Ampicillin Drug by Diperiodatoargentate (III) in Aqueous Alkaline Medium. *J. Phys. Org. Chem.* **2009**, *22*, 234.
(29) Fawzy, A. Removal of Toxic Tellurium (IV) Compounds via Bioreduction using Flucloxacillin in Aqueous Acidic Medium: A Kinetic and Mechanistic Approach. *J. Mol. Liq.* **2019**, *292*, 111436.
(30) Jose, T. P.; Nandibewoor, S. T.; Tuwar, S. M. Osmium(VIII) catalyzed oxidation of a sulfur containing amino acid-a kinetics and mechanistic approach. *J. Sulfur Chem.* **2006**, *27*, 25.
(31) Devra, V.; Yadav, M. B. Kinetics and Mechanism of Osmium(VIII) Catalyzed Oxidation of Valine by Hexacyanoferrate in Alkaline Medium. *Rassian J. Chem.* **2012**, *5*, 6773.
(32) Leal, J. M.; Garcia, B.; Domingo, P. L. Outer-Sphere Hexacyanoferrate (III) Oxidation of Organic Substrates. *Coord. Chem. Rev.* **1998**, *173*, 79.
(33) Farokhi, S. A.; Nandibewoor, S. T. Kinetic Mechanistic and Spectral Studies for the Oxidation of Sulfanilic Acid by Alkaline Hexacyanoferrate(III). *Tetrahedron* **2003**, *59*, 7595.
(34) Asghar, B. H.; Altass, H. M.; Fawzy, A. Copper(II) Catalysis for Oxidation of L-Tryptophan by Hexacyanoferrate(III) in Alkaline Medium: A Kinetic and Mechanistic Approach. *J. Saudi Chem. Soc.* **2017**, *21*, 323.
(35) Fawzy, A. Palladium(II)-Catalyzed Oxidation of L-Tryptophan by Hexacyanoferrate(III) in Perchloric Acid Medium: A Kinetic and Mechanistic Approach. *J. Chem. Sci.* **2016**, *128*, 247.
(36) Vovk, A. I.; Muraveva, I. V.; Kukhar, V. P.; Baklan, V. F. Kinetics of Oxidation of Vitamin B1 and Its Oacyl Analogs with Ferricyanide. A Mechanistic Model of Thiamin-Binding Protein. *Russ. J. Gen. Chem.* **2000**, *70*, 1108.
(37) Jose, T. P.; Angadi, M. A.; Salunke, M. S.; Tuwar, S. M. Oxidative Study of Gabapentin by Alkaline Hexacyanoferrate(III) in

https://dx.doi.org/10.1021/acs.iecr.0c03956
Ind. Eng. Chem. Res. 2020, 59, 16217−16224

Room Temperature in Presence of Catalytic Amount of Ru(III). A Mechanistic Approach. *J. Mol. Struct.* **2008**, *892*, 121.
(38) Durgannavar, A. K.; Patgar, M. B.; Chimatadar, S. A. Oxidation of Amoxicillin by Hexacyanoferrate(III) in Aqueous Alkaline Medium − A Kinetic and Mechanistic Approach. *Indian J. Chem., Sect. A: Inorg., Bio-inorg., Phys., Theor. Anal. Chem.* **2015**, *54A*, 1085.
(39) Vogel, A. I. *A Text Book of Practical Organic Chemistry: Including Quantitative Organic Analysis*; Longman: London, 1973.
(40) Stewart, R.; van der Linden, R. The Mechanism of the Permanganate Oxidation of Fluoro Alcohols in Aqueous Solution. *Discuss. Faraday Soc.* **1960**, *29*, 211.
(41) Laider, K. J. *Chemical Kinetics*; McGraw-Hill: New York, 1965.
(42) Michaelis, L.; Menten, M. L. The Kinetics of Invertase Action. *Biochem. Z.* **1913**, *49*, 333.
(43) Hicks, K. W.; Toppen, D. L.; Linck, R. G. Inner-Sphere Electron-Transfer Reactions of Vanadium(II) with Azidoamine Complexes of Cobalt(III). *Inorg. Chem.* **1972**, *11*, 310.

https://dx.doi.org/10.1021/acs.iecr.0c03956
Ind. Eng. Chem. Res. 2020, 59, 16217−16224