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Mechanistic Study on the Oxidation of 4-Hydroxycoumarin by Diperiodatonickelate(IV) in Aqueous Alkaline Medium

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Abstract: The oxidation of 4-hydroxycoumarin (HDC) by diperiodatonickelate(IV) (DPN) in aqueous alkaline medium at a constant ionic strength of 1.0 mol dm^{-3} was studied spectrophotometrically at 298 K. The reaction between DPN and 4-hydroxycoumarin in alkaline medium exhibits 1:3 stoichiometry (HDC: DPN). The reaction is of first order in [DPN] and has less than unit order in [HDC] and fractional order in [alkali]. The oxidation reaction in alkaline medium has been shown to proceed via a DPN- 4-hydroxycoumarin complex, which decomposes slowly in a rate-determining step followed by other fast steps to give the products. The main products were identified by spot test, IR, ^1H NMR studies. The reaction constants involved in the different steps of the mechanism were calculated. The activation parameters with respect to slow step of the mechanism were computed and discussed and thermodynamic quantities were also determined.

Keywords: Oxidation, Mechanism, 4-Hydroxycoumarin, Diperiodatonickelate(IV).

Introduction

The use of diperiodatonickelate(IV) (DPN) as an oxidant in an alkaline medium is restricted to a few cases due to its limited solubility and stability in aqueous medium¹⁻⁵. Reduction of nickel(IV) complexes has received a considerable attention to understand the nature of intermediate oxidation states of nickel such as nickel(III). Indeed, stable nickel(III) complexes are known⁶⁻⁷. Moreover, when nickel(IV) periodate is oxidant, it needs to be known which of the species is the active form of oxidant, since multiple equilibria between the different nickel(IV) species are involved.

The biological importance of coumarin derivatives as anticoagulants, aflatoxins, mycotoxins and antibiotics has led to a considerable amount of synthetic work in the field of coumarin for their pharmacological evaluation. 4-Hydroxycoumarin (4-hydroxy-2H-1-benzopyran-2-one) (HDC) is used in the synthesis of pharmaceuticals especially for anticoagulants. It is used in the manufacturing fluorescent dyes and rodenticides. The 4-hydroxycoumarin derivative, mercamour, is a long oral anticoagulant activity is in the duration of 48-72 hours. Ichikawa *et al*⁸ reported that 4-hydroxy-3-sulphonamidocoumarins are used as antibacterial and antitubercular agents.

In earlier reports⁴⁻⁵ on DPN oxidation, periodate had a retarding effect and order in the [alkali] was found to be less than unity in almost all the reactions and monoperodatonickelate(IV) (MPN), is considered to be the active species. However, in the present study we have observed entirely different kinetic observations and diperiodatonickelate(IV) (DPN) itself is found to be active form of the oxidant. The literature survey reveals that there are no reports on the mechanistic study of oxidation on 4-hydroxycoumarin by DPN. Thus, in order to explore the mechanism of oxidation by DPN in alkaline medium and to check the reactivity of hydroxy compounds towards DPN, we have selected 4-hydroxycoumarin as a substrate. The title reaction is studied to investigate the redox chemistry of the nickel(IV) in such media and to arrive at a plausible mechanism.

Experimental

All chemicals used were of reagent grade. Double distilled water was used throughout the experiment. The solution of 4-hydroxycoumarin (M/s. S.S. Antibiotics Pvt. Ltd., Aurangabad, India) was prepared by dissolving appropriate amount of recrystallised sample (from aqueous acetone) in alkali. The solid complex nickel(IV) periodate was prepared by known method⁹. The purity of the complex was checked by its UV-vis spectrum, which shows a broad absorption band at 410 nm. Aqueous solution of DPN was obtained by dissolving the solid complex in 1.0 mol dm⁻³ KOH solution. The Ni(IV) in alkaline solution was estimated gravimetrically¹⁰ after reducing it to Ni(II) and precipitating Ni(II) as its dimethyl glyoxime complex. Periodate solution was prepared by weighing out the required amount of a sample potassium periodate in hot water and was used after keeping for 24 hours to attain the equilibrium. Its concentration was ascertained¹¹ iodometrically at neutral pH maintained by a phosphate buffer. Nickel(II) solution was prepared from nickel sulphate (Fischer). Potassium hydroxide and potassium nitrate were employed to maintained required alkalinity and ionic strength respectively. Since, periodate is present in excess in the DPN complex, the possibility of 4-hydroxycoumarin oxidation by periodate in aqueous alkaline medium has been tested. The results indicated that the reaction between IO₄⁻ and 4-hydroxycoumarin is negligibly slow compared to the rate of reaction between DPN and 4-hydroxycoumarin under the experimental conditions.

Kinetic measurements

Kinetic measurements were performed on a Hitachi 150-20 spectrophotometer. All kinetic runs were followed under pseudo-first order conditions with the 4-hydroxycoumarin concentrations in excess over that of the oxidation at 25±0.1 °C, unless otherwise stated. The reaction was initiated by mixing thermally equilibrated solutions of DPN and 4-hydroxycoumarin, which also contained a definite quantity of KOH, KNO₃ and KIO₄. Here the total concentration of hydroxide ion was calculated considering the KOH in DPN as well as the KOH additionally added. Similarly, the total mataperiodate concentration was calculated by considering the amount present in the DPN solution and that additionally added. The course of reaction was followed by measuring the absorbance of unreacted DPN in the reaction mixture

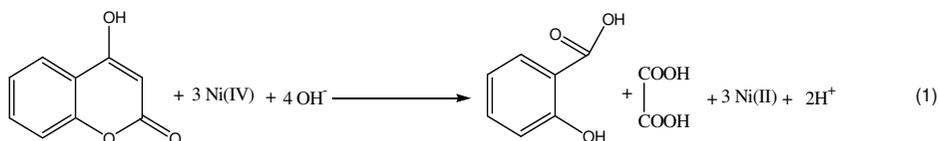
in a 1 cm quartz cell located in the thermostatted compartment of a spectrophotometer, at its maximum absorption wavelength of 410 nm as a function of time. Earlier, it was verified that there is negligible interference from other species present in the reaction mixture at this wavelength. The obedience of Beer's law by DPN at 410 nm was verified earlier and the molar absorbance coefficient, ' ϵ ' was found to be $7500 \pm 375 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ at this wavelength. The reaction was followed to more than 80% completion. The first order rate constants, k_{obs} were calculated from the slopes of $\log [\text{DPN}]$ vs. time plots. The rate constants were reproducible to within $\pm 5\%$.

In view of the modest concentration of alkali used in the reaction medium, attention was also directed to the effect of the surface reaction vessel on the kinetics. Use of polythene or acrylic wares and quartz or polyacrylate cells gave the same results, indicating that the surface does have any significant effect on the reaction rates. Kinetic runs were also carried out in the nitrogen atmosphere in order to understand the effect of dissolved oxygen on the rate of the reaction. No significant difference in the results was obtained under a nitrogen atmosphere and in the presence of air. In view of the ubiquitous contamination of carbonate in the basic medium, the effect of carbonate was also studied. Added carbonate had no effect on the reaction rates. However, fresh solutions were, nevertheless, used while carrying out the kinetic study. Regression analysis of experimental data to obtain regression coefficient r and the standard deviation S , of points from the regression line, was performed with the Microsoft Excel program.

Results and Discussion

Stoichiometry and product analysis

Different reaction mixtures with different sets of concentrations of reactants, where $[\text{Ni(IV)}]$ was in excess over 4-hydroxycoumarin at constant amount of ionic strength, alkali and periodate were kept for about 6 hours at $25 \pm 0.1^\circ \text{C}$ in nitrogen atmosphere and in a closed vessel. The remaining $[\text{DPN}]$ was assayed spectrophotometrically by measuring the absorbance at 410 nm. The results indicated the 3 moles of DPN is consumed by 1 mole of 4-hydroxycoumarin as in equation (1).



The reaction product was extracted with ether and recrystallised from aqueous alcohol and the purity was checked by HPLC. This was identified as salicylic acid by its IR spectrum (KBr) from FTIR Spectrometer Nicolet Impact 410, which showed a band at (ν) 1701 cm^{-1} due to $\text{C}=\text{O}$ and 3392 cm^{-1} due to phenolic OH. Salicylic acid was further characterized by ^1H NMR spectrum from NMR Spectrometer Bruker-F300MHz ($\text{CDCl}_3 + \text{DMSO-d}_6/\text{TMS}$) δ , 5.74 (s, 1H, phenolic OH, D_2O exchangeable), 7.27-7.82 (m, 4Ar H), 11.5 (s, 1H, acidic OH, D_2O exchangeable). The other product was oxalic acid, which is highly soluble in water, was identified by spot test¹² and Ni(II) sulphate was identified by spot test¹³ and UV-Vis spectrum. It was observed that the salicylic acid and oxalic acid do not undergo further oxidation under the present kinetic conditions.

Reaction orders

The reaction orders were determined from the slope of $\log k_{obs}$ vs. \log (concentration) plots by varying the concentrations of 4-hydroxycoumarin, alkali and periodate in turn while keeping all other concentrations and conditions constant.

Effect of [diperiodatonickelate(IV)]

The oxidant DPN concentration was varied in the range of 1.0×10^{-5} to 1.0×10^{-4} mol dm⁻³ and the fairly constant k_{obs} values indicate that order with respect to [DPN] was one (Table 1). This was also confirmed by linearity of the plots of log [absorbance] vs. time ($r \geq 0.986$, $S \leq 0.014$) up to 85% completion of the reaction.

Effect of [4-hydroxycoumarin]

The effect of 4-hydroxycoumarin on the rate of reaction was studied at constant concentrations of alkali, DPN and periodate at a constant ionic strength of 1.0 mol dm⁻³. The substrate, HDC was varied in the range of 3.0×10^{-4} to 3.5×10^{-3} mol dm⁻³. The k_{obs} values increased with increase in concentration of 4-hydroxycoumarin (Table 1). The order with respect to [HDC] was found to be less than unity ($r \geq 0.995$, $S \leq 0.009$). This is also confirmed in the plots of k_{obs} vs. [HDC]^{0.51}, which is linear rather than the direct plot of k_{obs} vs. [HDC] in Figure 1.

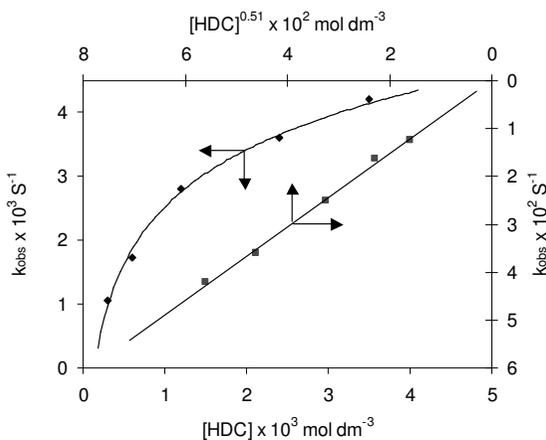


Figure 1. Plot of k_{obs} vs [HDC]^{0.51} and k_{obs} vs [HDC].

Effect of [alkali] and [periodate]

The effect of increase in concentration of alkali on the reaction was studied at constant concentrations of 4-hydroxycoumarin, DPN and periodate at a constant ionic strength of 1.0 mol dm⁻³ at 25 °C. The rate constants increased with increase in alkali concentration (Table 1), indicating fractional order dependence of rate on alkali concentration ($r \geq 0.988$, $S \leq 0.007$). The effect of periodate was observed by varying the periodate concentration from 1.0×10^{-5} to 1.0×10^{-4} mol dm⁻³ keeping all other reactant concentrations constant. It was found that the added periodate had no effect on the rate of reaction (Table 1).

Effect of dielectric constant of the medium (D) and ionic strength (I)

The relative permittivity (ϵ_T) effect was studied by varying the *t*-butanol-water content in the reaction mixture with all other conditions being constant. Attempts to measure the relative permittivity of the mixture of *t*-butanol-water were not successful. However, they were computed from the values of pure liquids¹⁴. The solvent did not react with the oxidant under the experimental conditions. The rate constants, increased with decreased in the dielectric constant of the medium. The plot of log k_{obs} vs. $1/\epsilon_T$ was linear with positive slope as shown in Figure 2 ($r \geq 0.9887$, $S \leq 0.013$). The effect of ionic strength was studied by varying the

potassium nitrate concentrations from 0.50 to 2.0 mol dm⁻³ at constant [DPN], [HDC], [OH⁻] and [IO₄⁻]. It was found that the rate constant increased with increase in concentrations of KNO₃ and the plot of log k_{obs} vs. √I was linear with positive slope, which is given in Figure 2 (r ≥ 0.988, S ≤ 0.007).

Table 1. Effect of [DPN], [HDC], [IO₄⁻] and [OH⁻] on diperiodatonickelate(IV) oxidation of 4-hydroxycoumarin alkaline medium at 25 °C, I = 1.0 mol dm⁻³.

[DPC] × 10 ⁴ , mol dm ⁻³	[HDC] × 10 ³ , mol dm ⁻³	[IO ₄ ⁻] × 10 ⁴ , mol dm ⁻³	[OH ⁻], mol dm ⁻³	k _{obs} × 10 ³ , s ⁻¹	k _{obs} × 10 ³ , s ⁻¹
0.1	1.2	0.1	0.5	2.52	2.60
0.3	1.2	0.1	0.5	2.54	2.60
0.6	1.2	0.1	0.5	2.50	2.60
0.8	1.2	0.1	0.5	2.49	2.60
1.0	1.2	0.1	0.5	2.55	2.60
0.6	0.3	0.1	0.5	1.25	1.20
0.6	0.6	0.1	0.5	1.63	1.80
0.6	1.2	0.1	0.5	2.50	2.60
0.6	2.4	0.1	0.5	3.60	3.50
0.6	3.5	0.1	0.5	4.20	4.10
0.6	1.2	0.1	0.5	2.50	2.60
0.6	1.2	0.3	0.5	2.54	2.60
0.6	1.2	0.5	0.5	2.56	2.60
0.6	1.2	0.8	0.5	2.52	2.60
0.6	1.2	1.0	0.5	2.54	2.60
0.6	1.2	0.1	0.1	9.91	9.91
0.6	1.2	0.1	0.3	7.83	7.83
0.6	1.2	0.1	0.5	7.12	7.12
0.6	1.2	0.1	0.8	6.61	6.61
0.6	1.2	0.1	1.0	6.13	6.13

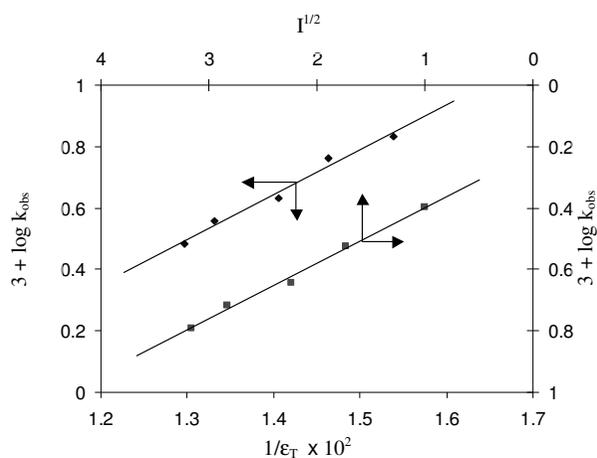


Figure 2. Effect of solvent polarity (ϵ_T) and ionic strength (I) on the oxidation of 4-hydroxycoumarin by diperiodatonickelate(IV) in aqueous alkaline medium at 25 °C.

Effect of initially added products

The externally added products, such as the nickel sulphate, oxalic acid and salicylic acid did not have any significant effect on the rate of the reaction.

Polymerization study

To test the intervention of free radicals, the reaction mixture was mixed with acrylonitrile monomer and kept for 4 hours under nitrogen atmosphere. On dilution with methanol, no precipitate was formed, indicating the absence of free radicals in the reaction.

Effect of temperature (T)

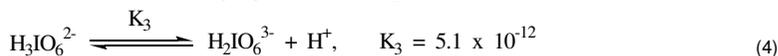
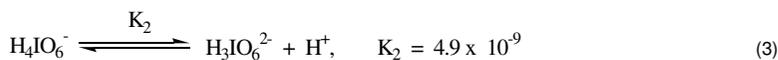
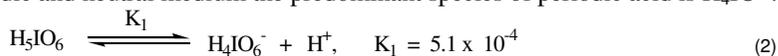
The kinetics was studied at four different temperatures (298, 303, 308 and 313) K under varying concentrations of 4-hydroxycoumarin alkali and periodate, keeping other conditions constant. The rate constants were found to increase with increase in temperature. The rate constants (*k*) of the slow step of Scheme 1 were obtained from the slopes and intercepts of $1/k_{\text{obs}}$ vs. $1/[\text{HDC}]$ and $1/k_{\text{obs}}$ vs. $[\text{OH}^-]$ plots at four different temperatures and were used to calculate the activation parameters. The energy of activation corresponding to these constants was evaluated from the Arrhenius plot of $\log k$ versus $1/T$ ($r \geq 0.976$, $S \leq 0.009$) and other activation parameters obtained are tabulated in Table 2.

Table 2. Thermodynamic activation parameters for the oxidation of 4-hydroxycoumarin by DPN in aqueous alkaline medium with respect to the slow step of scheme 2.

(A) Effect of temperature.	
Temperature, K	$k \times 10^3, \text{s}^{-1}$
298	4.45
303	6.10
308	7.80
313	8.70

(B) Activation parameters (Scheme 2).	
Parameters	Values
$E_a, \text{kJ mol}^{-1}$	35 ± 3
$\Delta H^\ddagger, \text{kJ mol}^{-1}$	32.0 ± 2
$\Delta S^\ddagger, \text{JK}^{-1} \text{mol}^{-1}$	-177 ± 16
$\Delta G^\ddagger, \text{kJ mol}^{-1}$	46 ± 4
log A	11.0 ± 1

The water soluble^{6,7} nickel(IV) periodate complex is reported^{5,15-16} to be $[\text{Ni}(\text{HIO}_6)_2(\text{OH})_2]^{6-}$. Although periodate is involved in multiple equilibria (2)-(4), which prevail to varying extents depending on the pH employed, under the strong alkaline conditions of the study (pH 13.3) the predominant form of periodate is expected to be $\text{H}_3\text{IO}_6^{2-}$ and not HIO_6^{4-} , which appears in present in the Ni(IV) complex^{4-5,15-16}. On the contrary, in mild acidic and neutral medium the predominant species of periodic acid is H_4IO_6^6 .



the complex formation between DPN and 4-hydroxycoumarin, which explains the less than unit order dependence on [HDC]. Scheme 1 leads to the rate law,

$$\text{rate} = - \frac{d[\text{DPN}]}{dt} = k K_4 K_5 [\text{HDC}] [\text{OH}] [\text{DPN(IV)}] \quad (5)$$

$$k_{\text{obs}} = \frac{\text{rate}}{[\text{DPN}]} = \frac{k K_4 K_5 [\text{OH}][\text{HDC}]}{1 + K_4[\text{OH}] + K_4 K_5 [\text{HDC}] [\text{OH}]} \quad (6)$$

This explains all the observed kinetic orders of different species. The rate law (6) can be rearranged in to the following form, which is suitable for verification:

$$\frac{1}{k_{\text{obs}}} = \frac{1}{k K_4 K_5 [\text{OH}][\text{HDC}]} + \frac{1}{k K_5 [\text{HDC}]} + \frac{1}{k} \quad (7)$$

According to equation (7), other conditions being constant, plots of $1/k_{\text{obs}}$ versus $1/[\text{OH}]$ ($r \geq 0.985$, $S \leq 0.014$), $1/k_{\text{obs}}$ versus $1/[\text{HDC}]$ ($r \geq 0.996$, $S \leq 0.012$) and should be linear and is found to be so in Figure 3. The slopes and intercepts of such plots lead to the values of K_4 , K_5 and k as $(1.30 \pm 0.05) \text{ dm}^3 \text{ mol}^{-1}$, $(3.1 \pm 0.2) \times 10^3 \text{ dm}^3 \text{ mol}^{-1}$, $(4.45 \pm 0.5) \times 10^{-3} \text{ s}^{-1}$ respectively. The value of K_4 is in good agreement with earlier literature¹⁹. These constants were used to calculate the rate constants and compared with the experimental values and found to be in reasonable agreement with each other (Table 1), which fortifies the Scheme 1.

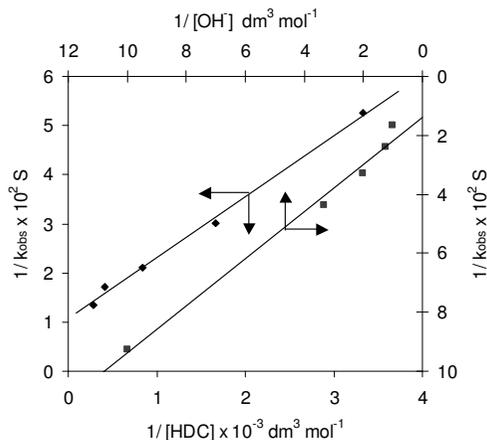


Figure 3. Verification of rate law (eq. 7). Plots of $1/k_{\text{obs}}$ vs. $1/[\text{HDC}]$ and $1/k_{\text{obs}}$ vs. $1/[\text{OH}]$ (conditions as in Table 1).

The effect of ionic strength and dielectric constant of the medium on the rate explains qualitatively the reaction between neutral and negatively charged ions, as seen in Scheme 1. The proposed mechanism is also supported by the moderate values of thermodynamic parameters. The fairly high positive values of the free energy of activation and enthalpy of activation indicate that the transition state is highly solvated, while ΔS^\ddagger suggests that the intermediate complex is more ordered than the reactants. The modest value of the enthalpy of activation and the higher rate constant of the slow step of the mechanism indicate as that an oxidation presumably occurs by an inner-sphere mechanism. This conclusion is supported by earlier observation²⁰.

Conclusion

Among various species of diperiodatonickelate(IV) in alkaline medium, DPN itself is considered as active species for the title reaction. The results indicate that, the role of pH in the reaction medium is crucial. Rate constant of slow step and other equilibrium constants involved in the mechanism are evaluated and activation parameters with respect to slow step of reaction were computed. The overall mechanistic sequence described here is consistent with product studies, mechanistic and kinetic studies.

Appendix

According to Scheme 1,

$$\text{Rate} = -\frac{d[\text{DPN}]}{dt} = k[\text{C}] = kK_4K_5[\text{HDC}]_f[\text{DPN}]_f[\text{OH}]_f \quad (\text{I})$$

$$[\text{DPN}]_t = [\text{Ni}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{2-} + [\text{Ni}(\text{OH})_2(\text{H}_3\text{IO}_6)(\text{H}_2\text{IO}_6)]^{3-} + [\text{C}]$$

where t and f refer to total and free concentrations.

$$[\text{Ni}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{2-}_f = \frac{[\text{DPN}]_t}{1 + K_4[\text{OH}] + K_4K_5[\text{HDC}][\text{OH}]} \quad (\text{II})$$

Similarly,

$$[\text{HDC}]_f = \frac{[\text{HDC}]_t}{1 + K_4K_5[\text{Ni}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{2-}} \quad (\text{III})$$

$$[\text{OH}]_f = \frac{[\text{OH}]_t}{1 + K_4[\text{Ni}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{2-} + K_4K_5[\text{Ni}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{2-}[\text{HDC}]} \quad (\text{IV})$$

Substituting the equations (II), (III) and (IV) in eqn. (I) (omitting the subscripts t and f) we get eqn. (V)

$$\text{rate} = \frac{kK_4K_5[\text{DPN}][\text{OH}][\text{HDC}]}{(1+K_4[\text{OH}]+K_4K_5[\text{HDC}][\text{OH}])(1+K_4K_5[\text{DPN}][\text{OH}])(1+K_4[\text{DPN}]+K_4K_5[\text{DPN}][\text{HDC}])} \quad (\text{V})$$

In view of low concentration of DPN used, the terms $([1+K_4K_5[\text{DPN}][\text{OH}]])$ and $(1+K_4[\text{DPN}]+K_4K_5[\text{DPN}][\text{HDC}])$ approximate to unity. Therefore,

$$k_{\text{obs}} = \frac{\text{rate}}{[\text{DPN}]} = \frac{kK_4K_5[\text{OH}][\text{HDC}]}{1 + K_4[\text{OH}] + K_4K_5[\text{HDC}][\text{OH}]} \quad (\text{VI})$$

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